In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 14-560V

(Filed: April 16, 2020)

JEAN YATES, *individually and as a representative of the late* ROBERT YATES,	*	To Be Published
Petitioner,	*	Denial of Entitlement; Meningococcal Conjugate ("Menactra") Vaccine; Lymphocytic Myocarditis; Death
v.	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	
Respondent.	*	

Patricia Finn, Esq., Patricia Finn, P.C., Piermont, NY, for petitioner.
Voris Johnson, Esq., U.S. Department of Justice, Washington, DC, for respondent.

DECISION[1]

Roth, Special Master:

On June 30, 2014, Jean Yates ("Ms. Yates," or "petitioner") filed a petition as representative for the estate of her deceased son, Robert Yates ("Robert"), for compensation under the National Vaccine Injury Compensation Program, 42 U.S.C. §300aa-10, et seq.[2] (the "Vaccine Act" or "Program"). The petition alleged that "[t]he death of Mr. Yates 'was caused in fact'" by a meningococcal conjugate ("Menactra") vaccination he received two days before on July 28, 2011.

[1] This Decision has been designated "to be published," which means I am directing it to be posted on the Court of Federal Claims' website, in accordance with the E-Government Act of 2002, Pub. L. No. 107-347, 116 Stat. 2899, 2913 (codified as amended at 44 U.S.C. § 3501 note (2006)). **This means the Decision will be available to anyone with access to the internet.** However, the parties may object to the Decision's inclusion of certain kinds of confidential information. Specifically, under Vaccine Rule 18(b), each party has fourteen days within which to request redaction "of any information furnished by that party: (1) that is a trade secret or commercial or financial in substance and is privileged or confidential; or (2) that includes medical files or similar files, the disclosure of which would constitute a clearly unwarranted invasion of privacy." Vaccine Rule 18(b). Otherwise, the whole Decision will be available to the public. *Id.*

[2] National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755. Hereinafter, for ease of citation, all "§" references to the Vaccine Act will be to the pertinent subparagraph of 42 U.S.C. § 300aa (2012).

Petition at 1, ECF No. 1.[3]

An entitlement hearing was conducted on July 27 and 28, 2017, in Washington, DC. Ms. Yates has suffered a tremendous loss due to the death of her son and the deepest sympathies are extended to her and her family. However, following careful review and analysis of all of the documentary evidence and testimony submitted in this case by both petitioner and respondent and in accordance with the applicable legal standards, I find that petitioner has not proffered sufficient evidence to demonstrate that the Menactra vaccination that Robert received on July 27, 2012 was the cause in fact or contributed to his death. Accordingly, I find that petitioner is not entitled to compensation.

I. Issues to be Determined

The issues to be determined are whether preponderant evidence exists to establish a reliable medical theory, a logical sequence of cause and effect, and a medically-appropriate temporal relationship between vaccination and Robert's death to prove that the Menactra vaccine administered on July 27, 2012 caused and/or contributed to Robert's myocarditis and death. *See* Jt. Sub. at 1-2.

A key fact in dispute is whether Robert suffered from lymphocytic myocarditis or eosinophilic myocarditis.

The parties agree that the medical records are "generally accurate." Jt. Sub. at 1. The parties agree that only the autopsy report suggested that Robert had a seizure on the day that he died and that "[a]ll other contemporaneous records…do not establish that Robert actually had a seizure on the day he died." *Id*.

II. Procedural History

The petition was filed on June 30, 2014 and assigned to Special Master Dorsey. ECF Nos. 1-2. Petitioner filed medical records through November of 2014. *See* Petitioner's Exhibits ("Pet. Ex.") 1-3, ECF No. 6; Pet. Ex. 4-5, ECF No. 10; Statement of Completion, ECF No. 11.

On February 5, 2015, respondent filed his Rule 4(c) Report ("Resp. Rpt.") advising against compensation in this matter. ECF No. 14. Respondent noted that the Petition did not state the correct date of vaccination. Resp. Rpt. at 1 n.1. Respondent further noted that Robert received his second Menactra vaccination on July 27, 2012 and requested "that petitioner file all medical records documenting [Robert's] receipt of the first Menactra vaccine." *Id*. at 3 n.3. Respondent noted that, on autopsy, "Robert had a mildly dilated right heart ventricle and mild hypertrophy of his left heart ventricle" and his "cause of death was listed as 'microlymphocytic myocarditis, natural.'" *Id*. at 4.

During a status conference on February 24, 2015, petitioner advised that she would be

[3] The Petition provided an incorrect date of vaccination; the contemporaneous medical records reflect that Robert received the allegedly causal Menactra vaccination on July 27, 2012, three days prior to his death. *See* Pet. Ex. 1 at 54.

filing the report of Dr. Chang, a cardiologist. Scheduling Order at 1, ECF No. 15. Special Master Dorsey noted that this matter involves a complex diagnosis, on which Dr. Chang may be well equipped to opine; however, should that not be the case, petitioner should consider obtaining an additional report from an infectious disease specialist or an immunologist. *Id*. The special master requested that all experts review and opine on the medical examiner's report and resulting conclusions. *Id*. She also raised the conflicting dates in the record for Robert's receipt of the Menactra vaccine. *Id*. at 1-2. Petitioner's counsel confirmed that the allegedly causal vaccine was administered on July 27, 2012, and that the first Menactra vaccine Robert received was given on August 25, 2005. *Id*. at 2.

On May 26, 2015, Petitioner filed an expert report from Dr. Anthony Chang along with Dr. Chang's curriculum vitae ("CV"). Pet. Ex. 6-7, ECF No. 20. On June 3, 2015, Petitioner filed supporting literature and an updated CV for Dr. Chang. Pet. Ex. 8, ECF No. 21; Pet. Ex. 9, ECF No. 22. On July 30, 2015, petitioner filed her Affidavit. Pet. Ex. 10, ECF No. 24.

On August 14, 2015, respondent filed a Motion for Extension of Time within which to file his expert report and requesting that petitioner provide the actual autopsy slides for respondent's expert pathologist to review; this motion was granted. ECF Nos. 25-26. On September 18, 2015, petitioner filed a status report advising of her efforts to secure the autopsy slides and the expected date of receipt. ECF No. 27. On October 2, 2015, petitioner filed a status report advising that the autopsy films were forwarded directly by Westchester County Medical Examiner's Office to respondent's counsel. ECF No. 29.

This matter was reassigned to me on October 22, 2015. ECF Nos. 30-31. On November 13, 2015, respondent filed the reports and CVs of Scott Yeager, M.D., a cardiologist, and Rebecca Folkerth, M.D., a pathologist. Respondent's Exhibits ("Resp. Ex.") A-D. ECF No. 33. On November 19, 2015, respondent filed medical literature via CD. Resp. Ex. A, Tabs 1-13, Resp. Ex. C, Tabs 1-4, ECF No. 34.

During a status conference on December 4, 2015, petitioner's counsel advised that she intended to file a report from a pathologist and a supplemental report from Dr. Chang. Scheduling Order at 1, ECF No. 35. Petitioner filed two Motions for Extensions of Time thereafter to file her expert reports, which were granted. ECF Nos. 36-37. On April 20, 2016, petitioner filed the supplemental expert report of Dr. Chang, an expert report and CV from Dr. Laurel Waters, and supporting medical literature. Pet. Ex. 11-17, ECF No. 38.

During a status conference on June 9, 2016, respondent's counsel advised that he would not be filing any additional expert reports. ECF No. 39. On July 7, 2016, the parties filed a joint status report suggesting hearing dates. ECF No. 40. A two-day entitlement hearing was set for July 27-28, 2017. *See* Prehearing Order, ECF No. 41.

On August 3, 2016, respondent filed a supplemental expert report from Dr. Yeager and supporting medical literature. Resp. Ex. E, Resp. Ex. E, Tab 1, ECF No. 43.

The parties filed their prehearing submissions. Pet. Brief, ECF No. 44; Resp. Brief, ECF No. 45; Jt. Sub., ECF No. 47; Pet. Reply Brief, ECF No. 49.

On July 26, 2017, the day prior to the hearing, chambers reached out to counsel regarding the results of a Luminex Virus Panel Assay believed to have been performed during Robert's autopsy. In her report, Dr. Folkerth wrote, "Virology: No detection of Influenza A, A/H1, A/H3, B, RSV A, RSV B, Parainfluenza 1, 2, and 3, Human Metapneumovirus, Rhinovirus, or Adenovirus (by Luminex Virus Panel Assay)." Resp. Ex. C at 3. In her supplemental report, petitioner's expert, Dr. Waters wrote, "Virology produced a negative Luminex Virus Panel Assay, specifically Influenza A, A/H1, A/H3, B; RSV A & B; Parainfluenza 1, 2 & 3; Human Metapneumovirus; Rhinovirus and Adenovirus. Bacteriology showed negative cultures for blood and an unspecified body fluid." Pet. Ex. 13 at 5. Dr. Waters concluded that the viral assay showed no viral infection. *Id*. Despite an exhaustive review of the medical records, the actual test results for the Luminex Virus Panel Assay could not be located. Respondent's counsel responded via email that he could not locate the results either. There was no response from petitioner's counsel.

Early in the hearing, the issue of the Luminex Virus Panel Assay referenced by both Dr. Waters and Dr. Folkerth was raised. Tr. 41-44. At that time, petitioner's counsel advised that she was going to wait for her cross-examination of Dr. Folkerth before advising the Court that, following my inquiry the previous day, she reached out to the medical examiner's office and was advised that a Luminex Virus Panel Assay was not performed. Tr. 105. Counsel did not think it necessary to advise the Court of her findings prior to hearing.

At that point, Dr. Folkerth advised that she was uncertain of where that information came from, conceding that no test results could be found in the medical records for this case, and her reference to it was clearly a mistake. Tr. 101, 106. She added that assay testing is standard in connection with autopsies but, having written her report over two years ago, she could not recall where the information came from, again admitting her mistake. Tr. 101. Dr. Waters admitted to having taken the information directly from Dr. Folkerth's report when writing her own report, never looking for the actual report to verify the information. Tr. 41-42.

Petitioner's counsel then moved to have Dr. Folkerth's report and testimony barred in totality. Tr. 102-03. Respondent's counsel offered to have any reference to the assay excluded completely from the case. However, petitioner's counsel continued to argue, refusing to have it excluded and demanding to know where Dr. Folkerth got the information. Tr. 103-04. I advised petitioner's counsel that since she received confirmation that the assay was never performed, neither side would get the benefit or detriment from the absence of results. Tr. 104. Petitioner's counsel continued to demand that Dr. Folkerth explain where the information came from, arguing that this mistake meant Dr. Folkerth had made other mistakes in her report and her opinions should be barred. Tr. 106. Despite discussion, petitioner's counsel refused to appreciate that, while Dr. Folkerth included the mistaken results in her statement of the autopsy findings, Dr. Waters not only included the information in her report without ever looking for or seeing the report, but more importantly relied on the results of a test she never actually reviewed in reaching her conclusion that the assay testing was negative for viral infection therefore the Menactra vaccine Robert received was the cause of his myocarditis and death.

I asked Dr. Folkerth if the assay testing could still be done on the pathology slides to determine if an infection was present. Tr. 142. She advised that, if the slides were sent to the CDC, the testing could be performed. Tr. 142. An Order was issued after the hearing for the slides to be

sent to the CDC for testing. *See* Scheduling Order, ECF No. 52.

On April 2, 2018, petitioner filed a status report stating she had been advised by the Westchester County Medical Examiner that the testing could not be done with the slides that still existed; the tissue slides that would be required for such testing were destroyed six months after Robert's death. Status Report, ECF No. 67. Petitioner's counsel again insisted that Dr. Folkerth's opinions were based on the nonexistent assay results and should be barred. *Id*. at 1-2. Petitioner requested a status conference to discuss filing a Motion to Strike Dr. Folkerth's expert report and testimony. *Id*. at 2.

The requested status conference was held on May 23, 2018 to again discuss the issue of the Luminex Virus Panel Assay referenced by Dr. Folkerth and relied on by Dr. Waters. Scheduling Order at 2, ECF No. 68. I again advised that Dr. Folkerth only documented the results of the assay in her case summary but did not base her opinion in this case on those results. *Id*., citing Resp. Ex. C at 5. On the other hand, petitioner's expert, Dr. Waters, not only relied on Dr. Folkerth's case summary without ever looking at the medical record herself to confirm whether an assay had been performed, but relied on the "results" of the assay to conclude that, because the viral assay showed no viral infection, the vaccine was the cause of the lymphocytic myocarditis and ultimately, Robert's death. *Id*., citing Pet. Ex. 13 at 5, 7.

I advised counsel that if I were to strike Dr. Folkerth's expert report and testimony, I would also strike Dr. Waters' report and testimony since Dr. Waters relied on the results of the assay in formulating her opinion in this matter. Scheduling Order at 2, ECF No. 68. Finally, I advised counsel that, since the assay was never performed and there was no proof of viral infection at the time of petitioner's Menactra vaccine, the issue is moot, with no benefit or detriment to either side. *Id*. In fact, the absence of the assay was a benefit to petitioner, since we did not have definitive proof that petitioner suffered from an illness that was the cause of his lymphocytic myocarditis. *Id*. I advised petitioner's counsel that I could not stop her from filing a Motion to Strike Dr. Folkerth's opinions and testimony, but the foregoing would be my opinion on such a motion. *Id*. Petitioner did not file that motion.

Counsel were asked if they wanted to file post-hearing briefs in this matter. Petitioner's counsel stated that she would like the opportunity to file a post-trial brief. Scheduling Order at 2, ECF No. 68. Petitioner was ordered to file her post-hearing brief by August 20, 2018; respondent's post-hearing brief was due 60 days thereafter. *Id*.

Following three extensions of time, petitioner filed her post-hearing brief on November 28, 2018. *See* Motion for Extension of Time, ECF No. 69; Non-PDF Order, issued Aug. 16, 2018; Motion for Extension of Time, ECF No. 70; Non-PDF Order, issued Oct. 19, 2018; Motion for Extension of Time, ECF No. 71; Non-PDF Order, issued Nov. 28, 2018; Pet. Post-Hearing Brief, ECF No. 72. Petitioner's post-hearing brief was missing citations to both the transcript and the medical literature; the caption was also incorrect. Scheduling Order at 1, ECF No. 73. Petitioner was ordered to file a Motion to Strike her post-hearing brief and refile a corrected copy. *Id*.

On December 3, 2018, petitioner filed a Motion to Strike her post-hearing brief; petitioner's Motion contained an incorrect caption. ECF No. 74. My chambers contacted petitioner via email

and requested that she move to strike and refile her Motion to Strike with the correct caption. *See* Order at 1, ECF No. 79. On December 4, 2018, petitioner filed a Motion to Strike both her post-hearing brief and her original Motion to Strike. ECF No. 75. An Order was issued granting this motion on December 6, 2018. ECF No. 79.

On December 5, 2018, petitioner filed a corrected copy of her post-hearing brief, an additional article of medical literature, the Menactra package insert, and an excerpt from a textbook discussing meningococcal disease. Pet. Ex. 25, ECF No. 76; Pet. Post-Hearing Brief, ECF No. 77; Pet. Ex. 26-27, ECF No. 78.

Respondent filed his post-hearing brief on January 29, 2019. Resp. Post-Hearing Brief, ECF No. 80. On March 5, 2019, petitioner filed a reply to respondent's post-hearing brief and an additional article of medical literature. Pet. Post-Hearing Reply, ECF No. 82; Pet. Ex. 28, ECF No. 83. Petitioner's reply was filed using the incorrect CM/ECF event, and she was instructed to file a Motion to Strike her reply brief. Later that day, petitioner filed a Motion to Strike, which was granted. ECF Nos. 84, 86. Petitioner then filed her reply brief as a "Response to Reply" brief. *See* ECF No. 85. Petitioner was advised that she had again filed her brief using the wrong CM/ECF event. *See* Order at 1, ECF No. 91. Petitioner was also informed that she was not authorized to file medical literature with her reply brief, and she would need to either obtain respondent's consent to file additional medical literature or file a Motion for Leave to Submit Additional Literature. *See id*. Petitioner was instructed to file a Motion to Strike both her reply brief and article of medical literature. *See id*. Petitioner filed this Motion on March 5, 2019; it was granted on March 12, 2019. ECF Nos. 87, 91.

On March 6, 2019, petitioner filed her reply brief as a "Notice." ECF No. 88. She filed a "Motion to Leave to File Attached Medical Literature Out of Time" on March 8, 2019. ECF No. 89. Petitioner submitted that the attached article, "Yamamoto et al.," was published in October of 2018 and was relevant to petitioner's claim because it observed lymphocytes in a case of eosinophilic myocarditis following a vaccine. *Id*. at 1. Respondent filed a response to this Motion on March 11, 2019, opposing petitioner's Motion. ECF No. 90. Respondent submitted that the article was irrelevant because it discussed eosinophilic myocarditis rather than lymphocytic myocarditis. *Id*. at 1. Respondent requested that, in the event that the special master granted petitioner's motion, respondent be allowed to file a written response from his expert addressing the article. *Id*. at 3.

On March 12, 2019, an Order was issued granting petitioner's motion based on Federal Circuit precedent requiring special masters to consider all relevant medical and scientific evidence of record. *See* Scheduling Order at 2, ECF No. 92 (citing *Moriarty ex rel. Moriarty v. Sec'y of Health & Human Servs*., 844 F.3d 1322, 1330 (Fed. Cir. 2016)).

Petitioner filed the Yamamoto article on March 18, 2019. Pet. Ex. 28, ECF No. 93. Respondent filed a supplemental report from Dr. Folkerth on April 9, 2019 addressing the article. Resp. Ex. F, ECF No. 94. An Order closing the record was issued on May 22, 2019. ECF No. 95.

This matter is now ripe for decision.

III. The Factual Record

A. Robert's Medical History Prior to the Menactra Vaccine

Robert was born on January 9, 1994. Pet. Ex. 1 at 10. His medical history included pervasive developmental disorder, "moderate to severe autism," and epilepsy. *Id*. at 10, 47; Pet. Ex. 2.2 at 6, 8. Prior to his receipt of the allegedly causal Menactra vaccine, Robert received all routine childhood vaccinations without event. Pet. Ex. 1 at 67-68.

The earliest record filed was April 7, 2009. Robert was presented to Dr. Selman at Blythedale Children's Hospital for neurologic evaluation. Pet. Ex. 5 at 5-6. He was a 15-year-old with known pervasive developmental disorder and familial history of same. *Id*. He did not have seizures. *Id*. He attended a special needs program, where he was learning keyboarding. *Id*. He could spell and understand spelled words, but his reading level was unknown. He had tantrums at school. *Id*. He exhibited several stereotypical behaviors, including shaking his hands, jumping, yelling, and rocking. *Id*. at 6. He could follow commands such as "give five" or "hold [your] arms up." *Id*. He took five mg of Valium[4] twice per day. *Id*. Dr. Selman asked for Robert's recent IEP, for a detailed tantrum diary to be kept, and for the school to provide the techniques being used to manage his physical outbursts. *Id*. Dr. Selman recommended re-evaluation during the summer of 2009. *Id*.

The next record was a phone call from Robert's father to the pediatrician, Dr. Barsh, on January 1, 2011. Robert now had a seizure disorder[5] and a refill of clonazepam[6] was needed. Pet. Ex. 1 at 8.

On February 11, 2011, emergency medical services were called to the Yates' home. Pet. Ex. 2.2 at 4. Upon arrival, EMS personnel found Robert on the stairs of his home, "somewhat subdued" and "moderately responsive." *Id*. He had reportedly had a seizure on the school bus. *Id*. EMS personnel deemed the home unsafe[7] and notified Child Protective Services ("CPS"). *Id*. Robert was transported via ambulance to Northern Westchester Hospital Center ("NWHC") Emergency Room. *Id*. at 6.

Dr. Bedi, the ER physician at NWHC, noted that Robert had a seizure disorder with a

[4] Valium is the brand name for diazepam, an anti-anxiety agent used to treat anxiety disorders; it can also be used as a skeletal muscle relaxant or anticonvulsant. *Valium*, DORLAND'S ILLUSTRATED MEDICAL DICTIONARY 2020 (32nd ed. 2012) [hereinafter "DORLAND'S"]; *diazepam*, *id.* at 512.

[5] There is a gap in the medical records between April 7, 2009 and January 1, 2011; accordingly, there is no indication of when Robert began having seizures.

[6] Clonazepam is an anticonvulsant used to treat atonic and myoclonic seizures. *Clonazepam*, DORLAND'S at 373.

[7] EMS personnel wrote, "Debris all over house w/ only narrow passageway throughout house. 2 other sons living in house – one witnessed living in "caged-off" area – no furniture/clothing." Pet. Ex. 2.2 at 4.

history of breakthrough seizures, for which he took Klonopin,[8] Keppra,[9] and Valium. Pet. Ex. 1 at 10. That day, Robert had a "brief, 10-second seizure" "while going to the school bus." *Id*. at 9, 10; Pet. Ex. 2 at 57. His parents gave him Klonopin, and the seizure stopped. *Id*. at 10. The bus driver had called the paramedics. *Id*.

Upon examination, Robert had redness, swelling, and healing bite marks on both wrists. Pet. Ex. 2 at 71. Blood work showed high glucose, sodium, hemoglobin, hematocrit,[10] eosinophils[11] at 7.2 (on a 0.0 to 6.0 scale), and low alkaline phosphatase,[12] MPV,[13] and lymphocytes.[14] Pet. Ex. 2.2 at 19, 21. Robert was given a fluid bolus;[15] follow-up with the neurologist was recommended. Pet. Ex. 1 at 9, 10. CPS agreed to allow Robert's parents to take him to a hotel while the home was being fixed. *Id*.; Pet. Ex. 2 at 57.

On March 28, 2011, Robert was presented to Dr. Barsh for several days of cough and fever. Pet. Ex. 1 at 13. He was taking 150 mg of Keppra twice per day and two 5 mg tablets of Valium twice per day. *Id*. He used Klonopin for seizures as needed. *Id*. Dr. Barsh prescribed 500 mg of Zithromax[16] daily for five days and recommended a follow-up in ten days if Robert was not better. *Id*.

---

[8] Klonopin is the brand name for clonazepam. *Klonopin*, DORLAND'S at 989.

[9] Keppra is the brand name for levetiracetam, an anticonvulsant medication used in the treatment of partial and myoclonic seizures and idiopathic generalized epilepsy. *Keppra*, DORLAND'S at 978; *levetiracetam*, *id*. at 1031.

[10] "Hematocrit" is an indirect measurement of red blood cell numbers and volume. It is used as a rapid measurement of red blood cell count. *See Mosby's Manual of Diagnostic and Laboratory Tests* 249 (Pagana eds., 6th ed. 2018) [hereinafter "*Mosby's*"].

[11] An eosinophil is a type of white blood cell that is involved in allergic reactions. *Mosby's* at 468. Eosinophils do not respond to bacterial or viral infections. *Id*. Increased eosinophil levels can indicate parasitic infection, allergic reaction, eczema, leukemia, or autoimmune disease. *Id*. at 473.

[12] Alkaline phosphatase ("ALP") is an enzyme concentrated in the liver and bones. *Mosby's* at 43-44. ALP levels are used to detect and monitor diseases of the liver or bone. *Id*. Low ALP levels can indicate low phosphate levels, malnutrition, milk-alkali syndrome, pernicious anemia, or vitamin C deficiency. *Id*.

[13] Mean Platelet Volume ("MPV") is a measure of the volume of platelets which varies with total platelet production. MPV is used to evaluate platelet disorders, including thrombocytopenia. *Mosby's* at 367. Low MPV levels can indicate aplastic anemia, chemotherapy-induced myelosuppression, or Wiskott-Aldrich syndrome. *Id*. at 368.

[14] A lymphocyte is a type of white blood cell that fights chronic bacterial infection and acute viral infections. *Mosby's* at 468-69. There are two types of lymphocytes, T-cells, which are involved in cellular-type immune reactions, and B-cells, which participate in antibody production. *Id*. at 468.

[15] A bolus is a single, relatively large quantity of a fluid or dose of a drug injected intravenously. *Bolus*, STEDMAN'S MEDICAL DICTIONARY 111520, accessed via WESTLAW EDGE (last visited Apr. 10, 2020).

[16] Zithromax is the brand name for azithromycin, an antibiotic used to treat mild to moderate bacterial infections. *Zithromax*, DORLAND'S at 2092; *azithromycin*, *id*. at 187.

On July 6, 2011, Robert presented to Dr. Sweeney for neurological follow-up. Pet. Ex. 1 at 15. His father reported that Robert had five seizures in the past month which lasted between three and five minutes. *Id*. During the most recent seizure, the convulsions caused Robert to hit his face on an end table and bleed. *Id*. He was given clonazepam melt-away tablets on his tongue, which helped. *Id*. It was hard to tell if he was incontinent as he was not toilet trained. *Id*. Robert's father reported that weather changes and heat brought on seizures. *Id*. He further reported that Robert had not been sleeping well due to changes in the home; he had a new bedroom, a new bed, and a new computer. *Id*. He was taking 5 mg of Valium four times per day, one mg of clonazepam at bedtime, and Keppra twice daily. *Id*. He was minimally interactive but awake, alert, and cooperative. *Id*. The plan was to increase Keppra to 2000 mg twice per day. *Id*. at 16. Blood work showed elevated eGFR[17] and SGPT (ALT).[18] *Id*. at 18. Eosinophils were normal, at 4.3 on a scale of 0.0 to 6.0. *Id*. at 17. A1C[19] and glucose levels were also normal. *Id*. at 14.

One week later, on July 13, 2011, Robert was presented to Dr. Barsh for an upper respiratory infection. Pet. Ex. 1 at 19. His mother reported drooping of the right eye, "almost like a Bell's palsy," that morning. *Id*. There was no history of tick bites or rashes. Examination was normal. *Id*. Dr. Barsh wrote, "I am glad to say Robert does not have a Bell's palsy. We are going to do a Lyme titer. No treatment is needed for his upper respiratory infection. *Id*. The Lyme Titer-Western blot came back EIA positive, but the IgM was negative with no bands, which according to the criteria was considered a negative test. *Id*. at 20-22.

Robert returned to Dr. Barsh one week later, on July 20, 2011, for his 17-year-old checkup. Pet. Ex. 1 at 25. He attended a special education program at the high school to learn computers. *Id*. He slept better when he had school the next day but would stay up late on other nights. *Id*. He enjoyed electronic games, walking, and staying busy outside. *Id*. He was taking 2000 mg of Keppra twice a day and Klonopin as needed. His A1C had been 5.5 but was improving with diet. *Id*. He was deemed a healthy 17-year-old with autism spectrum disorder. *Id*. Follow up with neurology for seizure disorder was advised. *Id*.

On July 22, 2011, Dr. Sweeney's neurology practice noted that Robert had a seizure the day before. His Keppra was increased to 2500 mg in the morning and 2000 mg at night. Pet. Ex. 1 at 26.

---

[17] eGFR stands for "estimated glomerular filtration rate." It is a test that measures the level of kidney function. *Estimated Glomerular Filtration Rate (eGFR)*, NATIONAL KIDNEY FOUNDATION, https://www.kidney.org/atoz/content/gfr (last visited Mar. 23, 2020).

[18] Alanine aminotransferase ("ALT"), also known as serum glutamic-pyruvic transaminase ("SGPT"), is an enzyme found predominantly in the liver. *Mosby's* at 36. ALT levels are used to identify liver diseases. Mildly increased ALT levels can indicate pancreatitis, myocardial infection, infectious mononucleosis, or shock. *Id*. at 37. Moderately increased ALT levels can indicate cirrhosis, severe burns, muscle trauma, liver tumor, obstructive jaundice, cholestasis, or presence of drugs toxic to the liver. *Id*. Significantly increased ALT levels can indicate hepatitis, liver necrosis, or ischemia of the liver. *Id*.

[19] The test for glycosylated hemoglobin, colloquially referred to as "A1C," is used to diagnose and monitor diabetes treatment. It provides an accurate long-term index of the patient's average blood glucose level. *Mosby's* at 238.

On September 23, 2011, Robert was presented to Dr. Barsh with hematuria. Pet. Ex. 1 at 28. Upon exam, he did not have bellyache, backache, or fever, and had no signs of kidney stones. *Id*. Prescriptions for Keppra, Valium, and clonazepam were written and given to Robert's father. *Id*.

On November 2, 2011, prescriptions for Keppra and clonazepam rapid dissolve tabs were given to Robert's father. *Id*.

On November 18, 2011, Robert was presented to Dr. Barsh for a contusion of the right foot. Pet. Ex. 1 at 30. An x-ray showed no fracture. *Id*. at 30-31.

On December 28, 2011, Robert was presented to Dr. Ratner at Mount Kisco Medical Group for vomiting, nasal congestion, and being "a bit out of sorts." Pet. Ex. 1 at 32. His dad was concerned for strep throat; he also had a cut on his foot. *Id*. A rapid strep test was negative. *Id*. at 32-33. Dr. Ratner removed a splinter from Robert's foot and recommended that he soak his foot four times per day. *Id*. at 32.

On January 16, 2012, Robert was presented to Dr. Barsh for persistent cough and ear pain keeping him up at night for two weeks. Pet. Ex. 1 at 34. He had two breakthrough seizures which his father reported were usual when he had an infection *Id*. Chest and cardiac examination were normal. *Id*. There was no fever. *Id*. Amoxicillin for ten days was prescribed for a possible sinus infection. *Id*.

Robert returned to Dr. Barsh on January 23, 2012, following completion of the amoxicillin. Pet. Ex. 1 at 35. He was still coughing; he also had dry skin behind both knees, moles on his back, and breakthrough seizures. *Id*. Dr. Barsh's impression was seizures, dermatitis, and moles; he recommended a referral to Dr. Mattison for a mole check and cortisone for the dermatitis. *Id*. Blood work revealed high cholesterol, high eGFR, low MPV, and eosinophils at 6.0 on a scale of 0.0 to 6.0, the high end of normal. *Id*. at 57-59. Robert was also vitamin D deficient. *Id*. at 57.

Robert returned to Dr. Barsh on January 27, 2012 with persisting cough. He was breathing comfortably. Pet. Ex. 1 at 36. He was prescribed 500 mg of Zithromax daily for five days and 50,000 units of Drisdol[20] once per week for 12 weeks for vitamin D deficiency. *Id*. A bone metabolism workup was recommended. *Id*.

On February 2, 2012, Robert was presented to Dr. Tsay for "severe vitamin D deficiency." Pet. Ex. 1 at 37. Dr. Tsay discussed with Robert's father the risk for "hungry bone syndrome"[21] and subsequent hypocalcemia following vitamin D replacement. *Id*. Dr. Tsay recommended supplementing with calcium for a few weeks and then rechecking Robert's vitamin levels. *Id*.

[20] Drisdol is the brand name for ergocalciferol, a sterol naturally occurring in fungi and some fish oils; it is administered orally or added to food as a source of vitamin D. *Drisdol*, DORLAND'S at 567; *ergocalciferol, id*. at 640.

[21] "Hungry bone syndrome" is the rapid deposition of calcium in bones which results in hypocalcemia. *Hungry bone s*., DORLAND'S at 1833.

On February 9, 2012, Robert was brought to the NWHC emergency room via ambulance after having a seizure on the school bus. Pet. Ex. 2 at 32, 35. EMS personnel reported that he was sluggish but awake upon their arrival. *Id*. at 32. He had a longstanding seizure disorder, severe autism, and was minimally verbal. *Id*. A chest x-ray showed right upper lobe perihilar infiltrate, likely suggestive of pneumonia. Pet. Ex. 1 at 39; Pet. Ex. 2 at 41. The heart was noted to be "prominent" on the x-ray. *Id*. Hospitalization was recommended, but Robert's father stated that hospitalization with restraints would be "disastrous." Robert was discharged with a prescription for Levaquin.[22] Pet. Ex. 2 at 33.

The next day, February 10, 2012, Robert was presented to Dr. Barsh for a follow-up. Pet. Ex. 1 at 40. He was taking 2500 mg of Keppra twice daily. *Id*. Seizures the day before and that day were noted. *Id*. Robert's dosage of Keppra was increased to five tablets in the morning and six tablets at night. *Id*. Dr. Barsh wrote, "We are not going to use a Levaquin (sic) that was prescribed in the ER right now. We are going to see how Robert does over the weekend." *Id*.

On February 22, 2012, Robert was presented Dr. Sweeney for a neurological follow-up for epilepsy and autism. Pet. Ex. 1 at 41. He was taking 2500 mg of Keppra in the morning and 3000 mg in the afternoon but had another seizure and his parents increased his Keppra, with an extra pill at night. *Id*. Robert's mother expressed concern about the number of moles Robert had and wanted his vision checked because he had been losing his footing when walking to the bus. *Id*. Robert's father reported that "there has been a slight change in the seizures. [Robert] does stiffen, and drool and shake, but he used to be tired afterwards. Now, dad states it is as if nothing happened, he just keeps going on his way." *Id*. Because Robert was on such a high dose of Keppra, Dr. Sweeney did not want to increase the dosage further. *Id*. at 41-42. She recommended continuing with one mg of clonazepam at night and 10 mg of Valium in the morning and at night. *Id*. at 42. Dr. Sweeney instructed Robert's parents to bring him back in six months for a follow-up. *Id*.

On March 30, 2012, a member of Dr. Tsay's staff entered a note of a telephone call with Robert's mother "to remind her [R]obert needs bloodwork done." Pet. Ex. 1 at 43.

On April 3, 2012, Dr. Barsh's staff made a note of "OT prescription mailed home." Pet. Ex. 1 at 44. The next day, it was also noted, "OT Rx mailed to Laurie Bauer at Bedford Central School District." *Id*. at 45. Another note entered on April 4, 2012, stated "Mr. Yates called for renewal of medications. As per Dr. Barsh, his Neurologist will be writting (sic) all RX's now, not Dr. Barsh. Mrs. Yates notified." *Id*. at 46.

On May 15, 2012, Robert was presented to Dr. McBride, a neurologist, for a second opinion for breakthrough seizures. Pet. Ex. 1 at 47. Dr. McBride noted that Robert was diagnosed with developmental delay during his first year of life with no history of febrile seizures, CNS infection, or head injury. *Id*. Robert's first seizure was in November of 2009; he had generalized tonic-clonic seizures lasting four minutes or less. *Id*. He was taking 2500 mg of Keppra in the morning and 3000 mg of Keppra at night but was still having breakthrough seizures. *Id*. He also took 10 mg of Valium at morning and at night, and one mg of clonazepam at night. *Id*. He had never had an EEG,

[22] Levaquin is the brand name for levofloxacin, a broad-spectrum antibiotic used to treat bronchitis, community-acquired pneumonia, urinary tract infections, acute maxillary sinusitis, and skin and soft tissue infections. *Levaquin*, DORLAND'S at 1031; *levofloxacin*, *id*. at 1032.

CT, or brain MRI. *Id*. Robert's brother also had autism and epilepsy. *Id*. Dr. McBride noted that it was uncertain whether Robert's epilepsy was generalized or secondary to pervasive development disorder but advised that he needed structural imaging and should have a brain MRI. *Id*. at 48. Dr. McBride ordered an MRI and an EEG and added 250 mg of Depakote[23] to Robert's regimen of seizure medications. *Id*. at 48-50. Dr. McBride instructed Robert's parents to bring him back for a follow-up and blood work in one month. *Id*. at 48. There were no records filed indicating that the ordered blood work was ever done.

There were some subsequent notes in Dr. McBride's records regarding Robert's medication. A May 18, 2012 note stated that generic Depakote could be used. Pet. Ex. 1 at 51. A June 29, 2012 note noted that prescriptions for clonazepam and Valium had an incorrect date; Dr. Barsh called Dr. McBride's office for permission to rewrite the prescriptions, which was granted. *Id*. at 52. A phone message from Robert's father on July 23, 2012 asked for a return phone call regarding a renewal of Keppra. *Id*. at 53. There was no indication of whether this call was returned.

Robert was returned to Dr. Barsh on July 27, 2012 for his 18-year-old examination. Pet. Ex. 1 at 54. Dr. McBride was following him for pervasive delay and epilepsy. Robert was taking Valium, Keppra, Depakote, and Klonopin. *Id*. He was noted to be a healthy 18-year-old with pervasive delays and epilepsy but doing well on his current medications. *Id*. Dr. Barsh encouraged Robert's father to speak to the school to ensure Robert had an hour of physical activity every day. *Id*. Blood work was ordered and a Menactra vaccine was administered after a discussion of the risks, benefits, and side effects was had with his father. *Id*. Blood work results showed positive Lyme titer, vitamin D deficiency, high cholesterol, high eGFR, high ALT, high MCHC,[24] low MPV, and high eosinophils of 9.4 on a scale of 0.0 to 6.0. *Id*. at 64-65.

B. Robert's Medical Records after the Menactra Vaccine.

On July 30, 2012 at 3:48 p.m., Pound Ridge Police Officer Thierstein was dispatched to the Yates' home for a report of an eighteen-year-old who was not breathing and had a history of seizures. Pet. Ex. 22 at 1. Upon arrival, Officer Thierstein was taken by Robert's brother to a bedroom where Robert's parents were administering CPR. *Id*. According to Officer Thierstein, Robert was unresponsive and did not appear to be breathing but did have a faint pulse. *Id*. Officer Thierstein "assembled the BVM[25] and connected it to high flow oxygen." *Id*. He instructed Mr. Yates to stop CPR so that he could use the BVM, but Mr. Yates refused. Mrs. Yates "stated that the only way that they were going to save their son was for [Mr. Yates] to continue giving breaths while she continued compressions. [Mrs. Yates] stated that this has happened before and that they have saved their son Robert Yates in the past by doing what they are doing." *Id*. The EMTs arrived and also tried to use the BVM, but Mrs. Yates refused, stating that "her husband could do a better

[23] Depakote is the brand name for divalproex sodium, a medication used in the treatment of epileptic seizures, particularly absence seizures. *Depakote*, DORLAND'S at 490; *divalproex sodium*, *id*. at 558.

[24] Mean Corpuscular Hemoglobin Concentration ("MCHC") is a measure of the average concentration of hemoglobin within a single red blood cell. *Mosby's* at 400. Elevated MCHC levels are usually attributed to alteration in red blood cell shape, which may confuse automated counting machines. *Id*. at 401.

[25] "BVM" stands for bag valve mask. *BVM*, NEIL DAVIS, MEDICAL ABBREVIATIONS 100 (16th ed. 2020).

job." *Id*. Robert was transported to NWHC by ambulance. *Id*. Officer Thierstein documented that Mrs. Yates "stated that this was not the first time something like this has happened but it was the most serious occasion to date." *Id*. She advised she had checked on Robert around 2:30 p.m. and he was sitting at his desk playing on the computer. *Id*. "[J]ust prior [to] the 911 call she checked on her son and he was slumped down in the chair at his desk and did not appear to be breathing." *Id*. Officer Thierstein's report documented that Trooper Yorke and Investigator Merritt responded to the scene to investigate. Their investigation reports were not filed into the record.

The ambulance record documents receipt of an emergency call at 3:48 pm and arrival at the Yates' home at 3:57 pm. Pet. Ex. 4 at 5. Robert was lying on the floor with CPR in progress. *Id*. Mrs. Yates reported that she "found patient slumped in front of his computer [and] pulseless apneic unconscious unresponsive. Unknown down time." *Id*. EMS personnel noted that Robert had pedal edema and his skin was cyanotic with delayed capillary refill. *Id*. Parents "tried to give patient lorazepam orally prior to EMS." *Id*. The EMTs were unable to intubate him due to a swollen tongue. *Id*. at 6. EKG showed asystole.[26] Epinephrine and sodium bicarbonate were administered, and CPR was continued during transport with no change. *Id*. The ambulance departed the Yates' home at 4:17 p.m. and arrived at NWHC at 4:31 p.m. *Id*. at 5. Despite extensive attempts at resuscitation in the ER, Robert was pronounced dead at 4:57 pm. Pet. Ex. 2 at 6-8. Robert's death certificate listed the immediate cause of death as lymphocytic myocarditis (pending further study). *Id*. at 4.

C. The Autopsy Report

The autopsy report documented an 18-year-old male with pervasive developmental disorder and generalized tonic-clonic seizures found unresponsive in his room at home. Pet. Ex. 3 at 13. His mother reported that he had a seizure that day and was given dissolvable clonazepam. *Id*. He had received a second dose of meningococcal vaccine on Friday, July 27, 2012. *Id*. His seizures were controlled with levetiracetam, diazepam, clonazepam, and Depakote. *Id*.

An examination of the heart showed mild hypertrophy of the left ventricle and mild dilation of the right ventricle. Pet. Ex. 3 at 13. Tissue samples were taken from the left ventricle, septum, and anterior, lateral, and posterior walls. *Id*. Microscopic examination of those samples showed evidence of subepicardial myocarditis; there was lymphocytic inflammatory infiltrate with focal myocyte necrosis.[27] *Id*. The report further noted interstitial fibrosis with scant lymphocytes. *Id*. There was no ischemia,[28] myocardial fiber hypertrophy, or fibrosis. *Id*. The other samples were unremarkable but for focal thinning and focal loss of striation of the myocardial fibers. *Id*. Tissue samples of the AV node were unremarkable and free of fibrosis, inflammation, granuloma, or

[26] Asystole is cardiac standstill or arrest; the absence of a heartbeat. *Asystole*, DORLAND'S at 170.

[27] The autopsy showed that there was inflammation of the outer muscular heart wall with deposits of white blood cells responsible for humoral and cellular immunity and sites of muscle cell death. *Myocyte*, DORLAND'S at 1222; *myocarditis*, *id*. at 1221; *necrosis*, *id*. at 1235; *lymphocyte*, *id*. at 1084; *infiltrate*, *id*. at 936.

[28] Ischemia is a deficiency of blood to a body part, usually due to functional constriction or actual obstruction of a blood vessel. *Ischemia*, DORLAND'S at 961.

tumor. *Id*. The lungs were normal; there was vascular congestion with fresh intra-alveolar hemorrhages. *Id*. The sections were free of inflammation, emphysema, fibrosis, or malignancy. *Id*. The bronchus and bronchioles were unremarkable. *Id*. There were fatty changes of the liver. *Id*.

The cause of death was lymphocytic myocarditis, natural. Pet. Ex. 3 at 10.

D. Mrs. Yates's First Affidavit and Testimony

Mrs. Yates submitted an affidavit prior to hearing and testified at hearing.

Mrs. Yates testified that she has four sons; two with autism. Tr. 11. Mrs. Yates stated Robert developed epilepsy at age 16, while her other son with autism developed epilepsy at 14; she believes it had something to do with puberty. Tr. 13. She affirmed that Robert had "some neurological issues and seizures" but "no serious or life-threatening illnesses." Pet. Ex. 10 at 1. He was healthy and under the care of physicians for his seizures. *Id*.

Mrs. Yates stated that Robert had good receptive language, but communicated as children with autism do, in different ways. Tr. 15. He would not tell her if he had a sore throat or a headache; "[i]t was up to me to guess first." Tr. 15-16. She could not take "their" temperature, referring to her "youngest children" with autism. Tr. 16.

According to Mrs. Yates on July 27, 2012, Mr. Yates picked up Robert from school after a half day and took him to the doctor for a routine physical. She was home with their other autistic son. Tr. 12-13; Pet. Ex. 10 at 1. Robert had blood taken and received his second Menactra vaccination at this appointment. Tr. 14-15; Pet. Ex. 10 at 1. She did not know the results of the blood work but believed it was normal, because she did not receive a telephone call stating otherwise. Tr. 14. Mrs. Yates affirmed, "Dr. Barsh gave a favorable medical report and recommended that [Robert] exercise for an hour a day at school. No medications were prescribed for [Robert]." Pet. Ex. 10 at 1. She affirmed that Robert came home with a Band-Aid. *Id*. She was not warned about any possible side effects of the vaccination. *Id*.

Mrs. Yates affirmed that the remainder of that day was normal, Robert spent time on the computer and watched television. Pet. Ex. 10 at 1. At hearing, she recalled Robert had received a Leapfrog book, a battery-operated book that reads to you, either that day or Saturday, and spent a lot of time using it. Tr. 17. She recalled nothing unusual the next day, July 28, 2012. Tr. 18-19. She then stated she was unsure which day it was, Saturday or Sunday, but Robert slept more than usual. Tr. 20. However, she sent him to school on Monday, which was a half day. She would not have sent him to school if he was not alright. Tr. 20-21.

According to Mrs. Yates on July 30, 2012, Robert came home from school around 12:30 p.m. and went to his room to play on the computer. Pet. Ex. 10 at 1-2. She looked in on him between 12:30 and 3:30 p.m., he was still on the computer. *Id*. at 2. When Mr. Yates came home around 3:30 p.m., she went to check on Robert and found him passed out with his headphones on seated at his computer with his head on the keyboard. The computer screen was black with the exception of a white square. *Id*. She screamed for Mr. Yates who came and started "mouth-to-mouth" while she did CPR. *Id*. Ian, her other son, made the emergency call. *Id*. The police arrived

with a balloon lung inflator, "but it was of no help." *Id*. Mr. and Mrs. Yates continued "our ministrations for about 45 minutes until the ambulance arrived" and took they Robert to NWHC. *Id*. Mr. Yates went in the ambulance with Robert, she stayed home with her other sons, Ian and Dylan. Tr. 22.

Mrs. Yates agreed that Robert's cause of death was lymphocytic myocarditis. Pet. Ex. 10 at 2.

Mrs. Yates stated that she filed a VAERS report but never heard from anyone. Tr. 26; Pet. Ex. 20. The VAERS report filed was consistent with Mrs. Yates' testimony; however, there was a letter attached to her filing showing a response addressed to her from VAERS. Pet. Ex. 20 at 3-4.

E. Mrs. Yates's Post-Hearing Affidavit

Petitioner submitted a second Affidavit following the hearing to address the contents of the police report.[29]

According to Mrs. Yates, Robert was never given CPR prior to July 30, 2012, nor was he ever taken to the hospital for a similar episode. ECF No. 63 at 1. "Robert was epileptic and on several occasions when he had an epileptic fit we would administer" clonazepam "and his epileptic fits would stop." *Id*.

Mrs. Yates recounted an occasion in 2006 when her son Dylan, who also has epilepsy, was admitted to NWHC and while there had another "fit" and Mr. Yates did CPR. ECF No. 63 at 1. The nurses encouraged Mr. Yates to continue doing the CPR, saying "Keep going! You are doing great!" *Id*. at 1-2. Dylan recovered from this episode. *Id*. at 2. Mrs. Yates affirmed, "I believe this is what the Pound Ridge police report is referring to when it states that I had made mention of Mr. Yates being able to save his son before by performing CPR." *Id*.

Mrs. Yates added that the BVM comes in two pieces and neither the police officer nor the EMTs appeared to know how to put it together. ECF No. 63 at 2. She and Mr. Yates had been doing CPR for several years by then. *Id*. They were not required to learn CPR or taught to perform CPR for any specific reason. *Id*.

IV. The Experts' Opinions

A. Petitioner's Experts

1. Dr. Anthony Chang

i. Qualifications

Dr. Anthony Chang is the director of the Heart Institute at Children's Hospital of Orange County. Pet. Ex. 9 at 3. He holds an undergraduate degree in molecular biology from Johns Hopkins University and a medical degree from Georgetown University Medical School. *Id*. at 1.

[29] Mrs. Yates' second affidavit was not filed as an exhibit and is cited herein as "ECF No. 63."

He did a fellowship in pediatric cardiology at the Children's Hospital of Philadelphia and worked as a cardiologist at Boston Children's hospital. Tr. 186; Pet. Ex. 9 at 1. He is board certified in pediatrics and pediatric cardiology. Pet. Ex. 9 at 2. Dr. Chang has been a cardiologist for over 30 years; he estimated that he consults on or sees 10 to 25 children with myocarditis per month, over a thousand cases per year. Tr. 186-87. He estimated that over the span of his career, he has dealt with anywhere from 3,000 to 10,000 cases of myocarditis or myocardial inflammation. Tr. 187. His areas of interest have included cardiac intensive care and heart failure in children; both areas deal with myocarditis of all types. Tr. 186. In addition to his clinical experience, Dr. Chang has written several manuscripts on myocarditis and coedited a supplement on myocarditis on behalf of the Pediatric Cardiac Intensive Care Society, which he founded. Tr. 186. Dr. Chang was also the chief editor of a 2006 textbook, *Heart Failure in Children and Young Adults: From Molecular Mechanisms to Clinical and Surgical Strategies*, in which he edited the chapter on myocarditis.[30] Tr. 186; Pet. Ex. 9 at 34.

In addition to his medical degree, Dr. Chang holds an MBA from University of Miami School of Business, an MPH from University of California at Los Angeles School of Public Health, and an MS in Biomedical Informatic/Artificial Intelligence from Stanford School of Medicine. *Id*.

ii. Causation Opinion

Dr. Chang opined that Robert suffered from myocarditis secondary to the Menactra vaccine. Pet. Ex. 6 at 2.

Dr. Chang explained that myocarditis is an inflammation of the heart muscle caused by different types of cells involved in fighting off infection or responding to a foreign substance. Tr. 188. The heart responds to inflammation by swelling; it becomes enlarged and less able to contract and relax normally. Tr. 188-89. If the inflammation affects the heart's conduction system, it can trigger a sudden cardiac event. Tr. 188-89. Inflammation of the heart can be acute, from within minutes to hours, to chronic, over months and years. The faster the onset of inflammation, the worse the patient's prognosis, because the changes in the heart's performance occur too quickly for the body to adapt. Tr. 189.

In Dr. Chang's opinion, Robert had an inflammatory response to the Menactra vaccine which led to a hypersensitivity or generalized inflammatory process that affected his heart and caused sudden cardiac arrhythmia and sudden cardiac death. Tr. 189.

Dr. Chang explained that Menactra vaccine induces an immune response using a weakened version of the bacteria, "so that when the real disease hits, the immune response is ready to attack the offending agent." Tr. 200. He stated anytime a foreign substance, medication, drug, or object is introduced into the body, you have an inflammatory response; usually the response is small, but sometimes it can be severe. Tr. 201-02. Dr. Chang has never seen an instance of a child dying of heart failure from a vaccine but has heard that cases of myocarditis have been reported secondary to the smallpox vaccine. Tr. 201.

Dr. Chang opined that, because Robert had previously received a Menactra vaccine in

[30] Petitioner did not file any excerpts from the chapter on myocarditis or this textbook into the record.

2005, his body had a biological memory for the vaccine, which caused him to have a more severe and accelerated reaction to the vaccine. This type of reaction could be referred to as a Type IV hypersensitivity response. Tr. 194-95. According to Dr. Chang, the elevated eosinophil count in Robert's bloodwork performed on the date that he received the second Menactra vaccine shows that the inflammation, or response to the vaccine, was already beginning. Tr. 192-93; *see also* Pet. Ex. 11 at 4 ("Of note, there was an elevated eosinophil count on the peripheral white blood cell profile (9.4%) to indicate that there is most likely a hypersensitivity inflammatory process that is generalized").

When asked how Robert could have had a hypersensitivity reaction when he had no symptoms of vomiting, swelling, difficulty breathing, or any other sign of an ongoing reaction, Dr. Chang responded, "

> Well, the heart sometimes…is the most vulnerable organ because it doesn't have sometimes a very active process to mediate the immune response. So, unfortunately, if the conduction system of the heart, the electrical wiring of the heart, is affected, unfortunately that could be lethal, even if it's not a severe inflammation that you'll see in the rest of the body."

Tr. 225.

Dr. Chang opined that Robert suffered from acute fulminant[31] myocarditis because "[t]he patient died in two to three days after administration of a substance." Tr. 210. He stated, "This is acute fulminant myocarditis, by definition, because the patient died within days of an onset of inflammation, and time course-wise, the only thing would make biomedical sense would be the vaccine." Tr. 217. A patient can have a hypersensitivity response, but still "have the same clinical diagnosis of essentially a very acute…fulminant clinically, acute fulminant myocarditis." Tr. 197. He characterized Robert's myocarditis as "acute fulminant myocarditis, plus/minus hypersensitivity, because of the rapid acceleration of the disease process…." Tr. 197.

In support of his theory, Dr. Chang submitted one case report in which a 17-year-old boy was admitted to pediatric intensive care with complaints of myalgias, chest pain, and low-grade fever two days after receipt of DTaP, meningococcal conjugate, and hepatitis A vaccinations and subsequently diagnosed with myocarditis. Pet. Ex. 8 at 1-2.[32] The authors noted that the possibility of a viral etiology could not be excluded even though there was a negative viral serology, but the absence of symptoms made it less likely. *Id*. at 2. It was further noted that, in cases of myocarditis reported after vaccination, a hypersensitivity reaction is usually suspected based on the temporal link between receipt of the vaccine or other offending agent and the onset of symptoms. *Id*. "Pathogenesis is related to a maladaptive immune response that leads to myocardial injury, as evidenced by biopsy specimens in cases of myocarditis after smallpox vaccination that have revealed $CD3^+$ T-cell infiltrate with prominent degranulating eosinophils." *Id*. at 2-3.

---

[31] "Fulminant" means sudden or severe; occurring suddenly and with great intensity. DORLAND'S at 748.

[32] Maria T. Thanjan et al., *Acute Myopericarditis After Multiple Vaccinations in an Adolescent: Case Report and Review of the Literature*, 119 PEDIATRICS e1400-03 (2007), filed as "Pet. Ex. 8," "Resp. Ex. A, Tab 11," and "Resp. Ex. C, Tab 4."

When asked if timing was the primary reason for his opinion that the vaccine was the cause of Robert's myocarditis and death, Dr. Chang initially denied that timing was the only reason but then stated, "but it would be one of the major supportive evidence for this being a reaction to the vaccine, that's correct." Tr. 211. Throughout the hearing, Dr. Chang repeatedly emphasized the significance of the temporal relationship between Robert's receipt of the Menactra vaccine and his sudden death. *See, e.g.,* Tr. 190 ("The clinical diagnosis in this case in terms of the time course is very, very relevant to the administration of the vaccine"), 195 ("…the response was very, very severe in a very short amount of time after a prior exposure to the vaccine"), 203 ("So the fact that [Robert] took two or three days is very, very consistent with…[an] acute reaction to the vaccine that is – that was so severe that it affected the heart to the degree that it did"), 205 ("…the timeline is extremely difficult to challenge that he responded to that severity to the vaccine").

Dr. Chang refused to differentiate between lymphocytic myocarditis and eosinophilic or hypersensitivity myocarditis and referred to what Robert suffered from as simply "myocarditis," stating myocarditis is a clinical diagnosis rather than a pathological diagnosis. Tr. 190, 191, 217. He maintained that, as a clinician, more emphasis is placed on treating the patient than labelling the type of myocarditis the patient suffers from. *See, e.g.,* Tr. 191 ("…it's not necessary to label myocarditis as a certain type of myocarditis…"), 192 ("If you want to call it hypersensitivity, you can. If you want to call it just an acute-onset myocarditis, you can also. No one would be right or wrong by labeling this differently…"), 197 ("…as a clinical cardiologist, we don't particularly care what label any doctor wants to put on the disease process. We have to treat the patient"), 199-200 ("You want to call it hypersensitivity, acute or acute fulminant myocarditis, to me [it] is just different experts debating about the label"), 216 ("I don't care what label you put on it, hypersensitivity versus – I can easily call this acute fulminant myocarditis"), 218 ("If you want to put a label of hypersensitivity on it, it doesn't – it doesn't make me want to treat the patient any different").

When asked about the distinction made in all of the medical literature that lymphocytic myocarditis is viral and eosinophilic myocarditis is hypersensitivity or indicative of allergic response, Dr. Chang stated, "I'm disagreeing with the gross oversimplification that you can necessarily and correctly put different patients into different categories that conveniently because not – I guarantee you that not 100 percent of patients are going to follow every single description for hypersensitivity myocarditis and not 100 percent of patients with lymphocytic myocarditis will follow all of that either." Tr. 204-05. He added, "If a patient responds to the vaccine in an accelerated and severe fashion that leads to essentially a sudden cardiac death, the type of cell is not going to tell you whether or not it is true or not that the patient responded to the vaccine because you can have a hypersensitivity kind of reaction without eosinophils." Tr. 208.

Dr. Chang disagreed with respondent's experts' opinions that a diagnosis of hypersensitivity myocarditis requires the presence of eosinophils in the heart tissue. He opined that the absence of eosinophils in the heart on autopsy does not preclude acute inflammatory myocarditis from vaccination. Pet. Ex. 11 at 4; Tr. 208. He added that hypersensitivity myocarditis is sometimes characterized by the presence of eosinophils, but it is not the only way that a hypersensitivity myocarditis can demonstrate itself. Tr. 190-91. A vaccination can trigger inflammation leading to either eosinophilic and/or lymphocytic myocarditis; both are inflammatory processes. Pet. Ex. 11 at 4. Although you can see eosinophils in a hypersensitivity

response, "not 100 percent of patients will have eosinophils in a hypersensitivity response to a vaccine…we don't have enough experience with vaccines and hypersensitivity situations [to know] what percent of the patients will actually have eosinophils." Tr. 194, 224.

Dr. Chang agreed that Robert's autopsy showed histopathological evidence of lymphocytic myocarditis, but in his opinion, a vaccine reaction can cause lymphocytes or eosinophils. Tr. 206, 208. He added, "…this is selected slices of the heart that did not show eosinophils. You can't just sort of make a blanket statement and say, well, because a number of slides did not show eosinophils, there were no eosinophils at all." Tr. 206. He added that, eosinophils or none, "this is acute fulminant myocarditis, by definition, because the patient died within days of an onset of inflammation, and time course-wise, the only thing that would make biomedical sense would be the vaccine." Tr. 216-17.

When asked for the literature which supported his statements that hypersensitivity myocarditis can be characterized histopathologically by lymphocytes, Dr. Chang referenced a 1992 abstract which was filed after the hearing. The abstract was a summary of a 1991 study which examined autopsy tissue specimens from 69 cases of hypersensitivity myocarditis to determine the association between the degree of cellular infiltration and cardiac symptoms. Pet. Ex. 24 at 1.[33] The authors defined hypersensitivity myocarditis "by the presence of eosinophils, a mixed lymphohistiocytic infiltrate along natural planes of separation, and an absence of fibrosis or granulation tissue in areas of infiltrate." *Id*. Examination of the cell types showed predominantly histiocytes, but lymphocytes were present in 12 cases and eosinophils in 30 cases. *Id*. The authors concluded that cardiac symptoms were not related to the degree of cellular infiltrate. *Id*.

Dr. Chang testified that, in determining that the Menactra vaccine caused Robert's myocarditis, he considered possible alternate causes. Robert did not have a congenital heart defect on autopsy. Tr. 212. He considered the effects of Depakote, agreeing that some anticonvulsant medications can cause hypersensitivity myocarditis. Tr. 199. He stated that it was "absolutely possible that there was some generalized inflammation that resulted" from the addition of Depakote to Robert's medication regimen in May of 2012 but added it was "two or three months before [Robert's] demise." Tr. 199. Therefore, he concluded that the Depakote was unlikely to be the "offending agent that led to [Robert's] inflammation and myocarditis" when compared to the "most obvious reason which is the administration of the vaccine." Tr. 199, 211-12.

Furthermore, Dr. Chang disagreed with respondent's position that Robert's myocarditis was caused by a viral infection.

While Dr. Chang agreed with Dr. Folkerth that lymphocytic myocarditis is most commonly caused by infection, he stated a finding of lymphocytes on autopsy does not dictate viral myocarditis as a cause of death. Tr. 208, 216. He referred to a study of autopsies of military personnel who did not die of myocarditis but still had lymphocytes in the heart on autopsy.[34] Tr. 215. In Dr. Chang's opinion, evidence of a low-grade viral infection on autopsy is "not a rare

[33] A.P. Burke et al., *Hypersensitivity Myocarditis*, 115 ARCH. PATHOL. LAB. MED. 764-69 (1991), filed as "Pet. Ex. 24."

[34] This study was not filed into the record for consideration.

finding…So it would be grossly erroneous for you to say, well, there are lymphocytes here so this patient died from viral myocarditis. That, I would be shocked if astute clinicians would say that." Tr. 215-16.

Rather, Dr. Chang stated the etiology of a patient's myocarditis should be based on the clinical history and other types of evidence, such as a viral panel and white blood cell count. Pet. Ex. 11 at 4. "I've never, ever seen a patient that dies from acute fulminant myocarditis from a virus, and yet was totally asymptomatic and had no infectious agent detected on any testing. That would be – that would be extremely rare." Tr. 198, 213. Dr. Chang added it is "theoretically possible" that Robert had a subclinical myocarditis that coincidentally developed at the same time the vaccine was received but it is "simply highly unlikely" because Robert's laboratory data and peripheral white blood cell count was "entirely normal without any supportive evidence of a viral infection." Pet. Ex. 11 at 4 (emphasis in original). Dr. Chang concluded that a diagnosis of hypersensitivity myocarditis "is now (sic) substantiated by the presence of these lymphocytes at the -- on the slides, in the specimen, but the time course, the presentation, the lack of any sign or symptom of viral infection makes it much more likely that this is a reaction." Tr. 191-92. "By far and away the most likely etiologic agent is the vaccine, not anything else." Tr. 213. Dr. Chang repeatedly stated that there was no sign of viral infection but did not address the fact that the Luminex Virus Panel Assay was never performed. Tr. 191, 197-98, 208, 211.

2. Dr. Laurel Waters

i. Qualifications

Dr. Laurel Waters received a Bachelor of Science from the University of California at Berkeley and a medical degree from the University of California at Davis. Pet. Ex. 19 at 1. She is board certified in pediatric pathology, nuclear medicine, and anatomic and clinical pathology.[35] *Id*. She is an assistant clinical professor at the University of California Davis School of Medicine in the Department of Pathology and Laboratory Medicine. Pet. Ex. 19 at 1. Dr. Waters described her duties at UC-Davis as "didactic and other types of teaching" rather than teaching students how to perform autopsies. Tr. 31. Although she has done "numerous" autopsies in her career, she has not performed an autopsy in "[a] couple of years," and was unsure of the last time she did an autopsy. Tr. 31, 33. In the past, she has probably reviewed "a dozen or so" slides on myocarditis. Tr. 34. Dr. Waters is not affiliated with, nor does she have privileges at, any hospital Tr. 32.

Dr. Waters also has a business in which she does expert witness work and medical/legal consultation; some of her work is for government agencies, and sometimes she consults with families to help them understand the process of disease and determine "whether they have a case or not." Tr. 31, 63. Consulting is about half of her income. Tr. 64. Dr. Waters does presentations but hasn't "been into publishing." Tr. 62.

Dr. Waters stated that in addition to her specialty in pediatric pathology, she has some background in immunology, having done some research in immunology through the early parts of

[35] A pathologist is a physician who interprets and diagnoses the changes caused by disease in tissues and body fluids. *Pathologist*, MERRIAM-WEBSTER ONLINE DICTIONARY, https://www.merriam-webster.com/dictionary/pathologist (last visited Mar. 23, 2020).

her career. Tr. 144. She has "kept up on immunology." Tr. 144. She stated, "I have an immunologist's kind of perspective as well as a pathologist kind of perspective." Tr. 144. She was asked to clarify her background in immunology, since her CV did not contain anything immunology related. Tr. 148. Dr. Waters stated that she did "a lot of research that involved cell-mediated cytotoxicity, looked at cytokines, lymphokines specifically; used a murine model where—asplenic murine model where I was doing in vitro tissue culture with mouse spleens." Tr. 148. She explained that this research was conducted during her training at UC-Davis in 1978 and UC-Berkeley in 1974. Tr. 148-49.

ii. Causation Opinion

Dr. Waters opined that Robert had an anamnestic T-lymphocyte cell response to the Menactra vaccine, which caused his myocarditis and subsequent death. Pet. Ex. 13 at 7. She explained that "[a]namnestic responses to a subsequent exposure to an antigen are quicker and more intense" noting Robert's prior Menactra vaccination in 2005. *Id*. at 3, 7. The Menactra vaccine is T-lymphocyte mediated, which, in Dr. Waters' opinion, correlates with the lymphocytic cells found in Robert's heart. *Id*. at 6-7. She further opined that his death three days after vaccination is consistent with other vaccine-caused myocarditis cases. *Id*. at 8.

Dr. Waters proposed that Menactra is a quadrivalent meningococcal polysaccharide protein conjugate; it is T-lymphocyte dependent, which means that the immune system responds to the vaccine by generating T-lymphocytes. Pet Ex. 13 at 5-6; Tr. 56. When asked to explain what this means, Dr. Waters testified, "

> …the body responds to Menactra by producing T-lymphocytes which have memory associated with—with the mixture of the protein and the polysaccharide that this vaccine had. The initial vaccines did not have the protein conjugate. And, so this was found to be much superior, but what—what happens is that there—that's just an explanation of what the mechanism of the body's response is to the vaccine and how it is mediated."

Tr. 87-88. After the hearing, Dr. Waters submitted a study containing the quote, "Meningococcal conjugate vaccines, through conjugation of polysaccharide to a protein carrier, changes the immune response from T-cell independent to T-cell dependent, leading to improved immunogenicity over polysaccharide vaccines." Pet. Ex. 21 at 1.[36] The study examined VAERS reports of pregnant women who received Menactra vaccinations; it did not identify any safety concerns. *Id*. at 1, 5.

Dr. Waters stated that myocardial inflammation can affect the atrioventricular node, which regulates heart rhythm via electrical stimulant; "involvement of the node can cause a dysrhythmia and sudden death." Tr. 38-39. Myocardial inflammation "may be due to lymphocytes and macrophages and [is] histologically termed lymphocytic myocarditis." Pet. Ex. 13 at 6. In her

[36] Yenlik Zheteyeva et al., *Safety of Meningococcal Polysaccharide-Protein Conjugate Vaccine in Pregnancy: a Review of the Vaccine Adverse Event Reporting System*, 208 AM. J. OBSTET. GYNECOL. 478.e1-6 (2013), filed as "Pet. Ex. 21."

report, Dr. Waters wrote, "[l]ymphocytes gravitated to the heart's conduction system causing a lethal arrhythmia and sudden death." *Id*. at 7. At hearing, she testified that, because Menactra works through a response of T-lymphocytes, "[t]he fact that we have a lymphocytic response is certainly very consistent with the cause being the vaccine and the time course is appropriate." Tr. 56-57. When asked if she had any evidence that the lymphocytes created in response to Menactra would gravitate to the heart's conduction system, Dr. Waters cited to a textbook excerpt which states "Myocarditis may be found in a significant number of cases of meningococcal sepsis, sometimes with involvement of the atrioventricular node." Pet. Ex. 18 at 8;[37] Tr. 73. However, this textbook discussed myocarditis from actual meningococcal bacterial disease and sepsis; it did not discuss the meningococcal vaccine. When asked whether she had any evidence specific to the Menactra vaccine, Dr. Waters responded, "I don't have that. As I said, I found it in the – in – since I found it in the package insert, I thought that was in the record." Tr. 73. The Menactra package insert, filed as Pet. Ex. 26, does not discuss whether lymphocytes created in response to Menactra would gravitate to the heart's conduction system. When asked if there was any literature supporting meningococcal vaccine causing lymphocytic myocarditis, Dr. Waters again referenced the Menactra package insert, stating the mechanism of action for the vaccine is through T-lymphocytes. Tr. 78. The package insert does not discuss myocarditis.

In her report, Dr. Waters noted that Robert's autopsy showed "a significant sized focus of inflammation in the heart which was primarily mononuclear with lymphocytes and macrophages… This is lymphocytic myocarditis, which is the most common histologic type of myocarditis." Pet. Ex. 13 at 4. Dr. Waters appeared to disagree with Dr. Chang's opinion that Robert suffered from an acute hypersensitivity myocarditis, noting "[t]his clinical pattern of myocarditis is shown under the microscope to have eosinophils" while "[t]he predominant cell type in Robert's heart was lymphocytes under the microscope, so it is histologically diagnosed as lymphocytic myocarditis." *Id*. at 7. When questioned, Dr. Waters agreed that histologically, there were only lymphocytes in Robert's heart on autopsy, with no evidence of eosinophils, but in an apparent attempt to agree with Dr. Chang, she added that a "clinical diagnosis of hypersensitivity myocarditis is not always accompanied by eosinophilic myocarditis under the microscope. It may have a predominance of lymphocytes, so that is not a way to separate out hypersensitivity." Tr. 35-36, 69.

Dr. Waters also discussed eosinophilic myocarditis in her report. She explained that "eosinophilic or hypersensitivity myocarditis…shows a mixed inflammatory cell infiltrate which includes eosinophils" and is sometimes associated with eosinophils in the peripheral blood. Pet. Ex. 13 at 6. She posited this is an allergic-type reaction; a person with this type of myocarditis may exhibit other clinical signs of allergic response. *Id*. She further stated that, clinically, when there is no peripheral eosinophilia, differentiating between lymphocytic and eosinophilic myocarditis depends on examination of the heart tissue by endomyocardial biopsy or autopsy. *Id*. At hearing, Dr. Waters agreed that it is possible to differentiate between lymphocytic myocarditis and eosinophilic myocarditis when examining tissue slides under a microscope. Tr. 35. She further conceded that evidence of eosinophils in heart tissue would indicate eosinophilic myocarditis, while the absence of eosinophils would preclude a finding of eosinophilic myocarditis. Tr. 149-50.

[37] ROGER W. BYARD, SUDDEN DEATH IN THE YOUNG 181-83, 197-99, 212, 215-16, 220, 256-57 (3rd ed. 2010), filed as "Pet. Ex. 18."

In support of her opinion that the Menactra vaccine caused Robert to suffer from lymphocytic myocarditis, Dr. Waters submitted the Ball[38] and Barton studies. Tr. 73-74, 75; Pet. Ex. 13 at 5-6; Pet. Ex. 16; Pet. Ex. 17.

Ball studied the safety of the meningococcal vaccine by examining reports of serious adverse events made through VAERS between 1990 and 1999. Pet. Ex. 16 at 2.[39] During that time, over six million doses of meningococcal vaccine were distributed in the U.S. and 264 adverse events were reported, 38 of which were considered serious. *Id*. at 2-3. Ball concluded that these statistics were "reassuring with regard to the safety of the meningococcal vaccine." *Id*. at 8. Of 11 reports of serious adverse events from outside the U.S., there was one report of myocarditis the day after immunization in an eight-year-old boy. *Id*. at 6. At hearing, Dr. Waters agreed that it was not determined whether that boy suffered from hypersensitivity or lymphocytic myocarditis. Tr. 74.

Barton was a case report on two children who developed eosinophilic myocarditis, one after meningococcal vaccination and one after hepatitis B vaccination. Pet. Ex. 17 at 1-2.[40] Both children manifested noncardiac symptoms the day of or the day after immunization and cardiac symptoms three to ten days after immunization. *Id*. at 4. Barton noted that eosinophilic myocarditis infrequently arises from allergic or autoimmune triggers and "has a distinctive pattern of eosinophilic inflammatory infiltrates that characterize the entity." *Id*. at 1. In both cases, a myocardial biopsy indicated eosinophilic myocarditis. *Id*. at 2-3.

Barton specifically stated that hypersensitivity myocarditis, which can occur after administration of various pharmaceutical agents, including vaccines, is characterized by a finding of eosinophilic infiltrate, "as opposed to a lymphocytic infiltrate, characteristic of viral etiology." Pet. Ex. 17 at 4. Barton further noted that other reports of cardiac injury associated with common vaccines supported an immune-mediated hypersensitivity mechanism. *Id*. However, Barton noted, "clinical, laboratory, and myocardial biopsy findings are indistinguishable between postvaccine and drug-induced myocarditis." *Id*. Patient Two received penicillin four weeks before vaccination and therefore a drug-induced myocarditis could not be excluded. *Id*.

Barton noted that one potential mechanism was a Type III hypersensitivity immune complex-mediated reaction, which usually occurs within one to two weeks of exposure. Pet. Ex. 17 at 4. Barton suggested that this mechanism was applicable to bacterial vaccines such as meningococcal vaccine, based on Patient Two's biopsy results showing immune complexes of meningococcal polysaccharide, IgG antibodies, and complement deposits in myocardial tissue and low serum complement. *Id*. Barton determined that the "characteristic eosinophilic infiltrate" present in both patients in this case report supported an allergic etiology. *Id*.

---

[38] The Ball study was incorrectly referred to as "Bell" in both Dr. Waters' report and at hearing. *See* Pet. Ex. 13 at 5; Tr. 74.

[39] Robert Ball et al., *Safety Data on Meningococcal Polysaccharide Vaccine from the Vaccine Adverse Event Reporting System*, 32 CLIN. INFECT. DIS. 1273-80 (2001), filed as "Pet. Ex. 16."

[40] Michelle Barton et al., *Eosinophilic Myocarditis Temporally Associated With Conjugate Meningococcal C and Hepatitis B Vaccines in Children*, 27 PEDIATR. INFECT. DIS. J. 831-35 (2008), filed as "Pet. Ex. 17."

Dr. Waters agreed that both patients discussed in Barton had myocardial biopsies showing eosinophilic infiltrate rather than lymphocytic infiltrate. Tr. 77-78. When asked to confirm that Barton found, to the extent that evidence existed for an association between myocarditis and the meningococcal vaccine, it would be eosinophilic, not lymphocytic myocarditis, Dr. Waters hedged, "[Barton] suggests that in two out of their two cases the eosinophilic part was histologically seen." Tr. 77-78. While Dr. Waters agreed that the eosinophilic infiltrate Barton found was caused by a hypersensitivity phenomenon, as opposed to lymphocytic infiltrate, which is characteristic of a viral etiology, she stated this only applies to a Type I hypersensitivity reaction, not the Type IV reaction she is opining occurred in Robert. Tr. 78-79.

Dr. Waters further agreed that the articles she relied on referred to eosinophilic myocarditis, not lymphocytic, when discussing vaccine-related myocarditis, but she stated basic textbooks state that vaccines can cause lymphocytic myocarditis. Tr. 80-81. When asked where those textbook references were in the record, she stated that she did not submit them because "it just seemed to be something that was so generally included in knowledge--" Tr. 81.[41]

Although not included in her written report, Dr. Waters opined at hearing that Robert suffered from a hypersensitivity reaction to the Menactra vaccine in agreement with Dr. Chang. Tr. 55-56. She based this opinion on the presence of lymphocytes in the myocardium, the lack of evidence of viral infection, and his death three days after vaccination. Tr. 55-56.

In Dr. Waters' opinion, the difference between a hypersensitivity response and lymphocytic myocarditis is that one term is histologic and the other is clinical. Tr. 76. Hypersensitivity myocarditis is a "clinical diagnosis" and can occur as an allergic or hypersensitivity response known as Type I, which involves eosinophils and the immunoglobulin IgE, or as a Type IV, which involves lymphocytes that react to viruses, "various toxins and so forth. And that's delayed type hypersensitivity." Tr. 35, 152.

More specifically, she stated Type I hypersensitivity reaction is evidenced by eosinophils and can occur within hours or it can extend out for days. Tr. 48, 51, 79. The reaction could have symptoms, but if it is not a "strong Type I reaction," the patient may not display eosinophils. Tr. 86. Dr. Waters offered the blood work performed the day of Robert's vaccination, stating it was "taken a few hours after" Robert received the second Menactra vaccine and showed elevated eosinophils consistent with a very rapid Type I response. Tr. 36, 54. She postured that, if an IgE level had been measured, it would have increased as well. Tr. 36. She stated Robert's eosinophil level on that day was 9.4%, a significant increase of 50% from his blood work six months earlier, which showed an eosinophil level of 6.0%, "at the upper limit of normal." Tr. 51-52. Dr. Waters relied on a 2017 study which defined the characteristics, treatment, and outcomes of eosinophilic myocarditis in the context of hypersensitivity reactions noting histologically, peripheral eosinophilia was absent in about 25% of patients with eosinophilic myocarditis. Pet. Ex. 25 at 1, 9.[42] "In particular, the high-risk group of patients with hypersensitivity eosinophilic myocarditis

[41] Petitioner was ordered to produce the textbooks that Dr. Waters referred to which state that vaccines can cause lymphocytic myocarditis. All of the literature filed post-hearing referred to eosinophilic myocarditis.

[42] Michaela Brambatti et al., *Eosinophilic Myocarditis Characteristics, Treatment, and Outcomes*, 70 J. AM. COLL. CARDIOL. 2363-75 (2017), filed as "Pet. Ex. 25."

with the highest occurrence of cardiac arrest and in hospital death can frequently lack peripheral eosinophilia (up to 35 to 40% of cases)." *Id*. at 9-10.

Dr. Waters was asked how the eosinophils in Robert's blood work could elevate so quickly from 6.0% to 9.4% when the blood work and vaccine were given at the same doctor's visit and around the same time. Tr. 59-60. She stated death from anaphylaxis due to eosinophils within minutes of exposure to an antigen by someone who is hyperallergic would cause the eosinophils to increase quickly. Tr. 60. She added that, while it was possible that Robert's medication was responsible for the rise in eosinophils, an acute increase to 9.4% on the same day as the vaccine would not have been from his medication. Tr. 60-61.

When asked how eosinophils played any role in Robert's myocarditis, Dr. Waters stated, "I didn't say they did…clinically because we had eosinophils there was an immediate hypersensitivity reaction. I didn't see any evidence in the heart, so it either subsided or it was seen elsewhere that I couldn't see." Tr. 70. "But it clearly does not rule out that there was an eosinophilic reaction earlier that we just don't see in the slides. That's very common that you will have a trenchant eosinophilic reaction and you might not see the eosinophils in the myocarditis -- in the heart slides that show myocarditis." Tr. 53.

When asked how Robert had elevated eosinophils in his blood testing but not on the autopsy slides, Dr. Waters responded that the autopsy slides were not done on day one "and it also takes some time for the eosinophils to infiltrate." Tr. 54. When asked how long it would take for eosinophils to infiltrate the heart, she stated, "That's a hard thing to study because it means you've got -- and, so, I don't think it's very clearly studied, because you would have to have times between an exposure to an antigen and then look at a biopsy. And doing endomyocardial biopsies is not a nontoxic thing to do. There's risks involved in it…You can't just do the biopsy, and obviously you would have to have a very complex study to do an autopsy study." Tr. 84-85.

Dr. Waters opined that a Type IV delayed hypersensitivity response, or "lymphocytic hypersensitivity response," is predominantly characterized by lymphocytes; it "never" has eosinophils. Tr. 36, 79. This type of reaction can take three days "when it's what we call an anamnestic response, where the antigen has been seen prior, so there are memory lymphocytes present so that they respond within a couple of days of the exposure." Tr. 48. In Dr. Waters' opinion, the fact that lymphocytes were seen on Robert's autopsy is "consistent with an anamnestic response for a type IV delayed-type hypersensitivity response because there are already memory cells there." Tr. 150. She added that Type IV reactions have a wide range of symptoms. Tr. 87.

When asked what literature she relied on in forming her opinion that hypersensitivity myocarditis can be characterized by only lymphocytes, Dr. Waters stated, "Cardiovascular pathology texts." Tr. 66. When further pressed, she stated, "I think it's at least inferred in the Byard – I think it may be in the Byard selection that I just submitted." Tr. 57. She was unable to find that excerpt at hearing. After the hearing, petitioner submitted Pet. Ex. 23, an excerpt from a pathology textbook.[43] The excerpt contains a "Figure 6-19" displaying two illustrations, (A) "Delayed-type

[43] ROBBINS AND COTRAN PATHOLOGIC BASIS OF DISEASE 206 (Vinay Kumar et al. eds., 8th ed. 2010), filed as "Pet. Ex. 23."

hypersensitivity and immune inflammation" and (B) "T cell-mediated cytolysis." Pet. Ex. 23 at 3. The caption reads:

> Mechanisms of T cell-mediated (type IV) hypersensitivity reactions. A. In delayed-type hypersensitivity reactions, CD4+ T_H1 cells (and sometimes CD8+ T cells, not shown) respond to tissue antigens by secreting cytokines that stimulate inflammation and activate phagocytes, leading to tissue injury. CD4+ T_H17 cells contribute to inflammation by recruiting neutrophils (and, to a lesser extent, monocytes). B. In some diseases, CD8+ cytotoxic T lymphocytes (CTLs) directly kill tissue cells.

Id. A paragraph below the caption reads "T Cell-Mediated (Type IV) Hypersensitivity – The cell mediated type of hypersensitivity is initiated by antigen-activated (sensitized) T lymphocytes, including CD4+ and CD8+ T cells (Fig. 6-19)." *Id*. The remainder of the text is cut off. Dr. Waters presumably relied on this textbook excerpt to support her theory that since Menactra is T-cell mediated it can cause this reaction. However, she provided nothing to explain how the vaccine could cause this, or if such findings were contained in the autopsy.

Dr. Waters also submitted Yamamoto after the hearing, a case report discussing biopsy-proven eosinophilic myocarditis related to tetanus toxoid vaccine. Pet. Ex. 28 at 1.[44] Yamamoto noted that the endomyocardial biopsy showed "unique histopathologic findings, characterized by perivascular eosinophilic infiltrates with myocyte necrosis and abundant interstitial lymphocytic infiltrates with myocyte necrosis." *Id*. "Immunoperoxidase staining revealed that the lymphocytic component consisted mostly of CD3+/CD4+ T cells, suggesting a type-IV delayed hypersensitivity reaction." *Id*. The biopsy findings led to a final diagnosis of acute eosinophilic myocarditis. *Id*. Yamamoto suggested that characterization of the inflammatory infiltrates in the biopsy sample may help to identify myocarditis etiology, noting that cases of smallpox vaccine-related myocarditis were "characterized by a prominent mixed eosinophilic and lymphocytic infiltrate." *Id.* at 4. Yamamoto further noted "another case of meningococcal C conjugate vaccine-related myocarditis suggested a type-III hypersensitivity reaction." *Id*. Yamamoto concluded that endomyocardial biopsy is a prerequisite for diagnosis and treatment of myocarditis. *Id*. Notably, while the patient in Yamamoto was suspected of having a Type-IV delayed hypersensitivity reaction, he or she had a "prominent" mix of eosinophils and lymphocytes on biopsy and was ultimately diagnosed with eosinophilic myocarditis rather than lymphocytic myocarditis.

Because Dr. Waters had agreed that lymphocytic myocarditis was commonly caused by a viral infection, she was asked to reconcile how a person with evidence of only lymphocytes on autopsy could be considered to have a clinical hypersensitivity myocarditis which requires eosinophils. She stated that lymphocytic myocarditis is not always caused by a virus; only half of lymphocytic myocarditis cases are viral and some of that association may be overblown because of the sensitivity of the tests used. Tr. 80. "There's plenty of lymphocytic myocarditis that can be seen following a bacteria (sic) or a toxin;" 9 to 17 percent of sudden death in children is the result of myocarditis and only 50% of those are viral. Tr. 37, 47. Therefore, half of the cases are unaccounted for. Where there is no evidence of viral infection and another cause exists, "one would

[44] Hiroyuki Yamamoto et al., *A Case of Biopsy-Proven Eosinophilic Myocarditis Related to Tetanus Toxoid Immunization*, 37 CARDIOVASC. PATHOL. 54-57 (2018), filed as "Pet. Ex. 28."

point to that other potential cause as the reason why we had the lymphocyte myocarditis." Tr. 57, 84.

In Dr. Waters' opinion, Robert fell into the 50% of lymphocytic myocarditis cases that are not caused by viruses. Tr. 84. When asked where the 50% came from Dr. Waters stated, "that's just sort of general knowledge." Tr. 84.

In her report, she relied on the "Luminex Assay results" to support her opinion that Robert did not have a virus. *See* Pet. Ex. 13 at 5 ("Virology produced a negative Luminex Virus Panel Assay, specifically influenza A, A/H1, A/H3, B; RSV A & B; Parainfluenza 1, 2, & 3; Human Metapneumovirus; Rhinovirus and Adenovirus. Bacteriology showed negative cultures for blood and unspecified body fluid"). At hearing, Dr. Waters was asked whether a positive result for viral infection on the Luminex Assay would have been dispositive as the cause of Robert's myocarditis. Tr. 81-82. Dr. Waters responded, "It -- unless it was one of those cases where [testing] was overdone, where there were only a few molecules seen, and it didn't make sense clinically." Tr. 82.

When asked whether Robert's lymphocytic myocarditis could have been caused by his pneumonia infection in February of 2012, Dr. Waters stated, "[C]ertainly that's possible, but…the studies that have done about viral infections and viral involvement with myocarditis" are "highly sensitive…and will pick up as few as ten molecules or ten organisms." Tr. 59. When asked if Robert had any symptoms of a hypersensitivity myocarditis, Dr. Waters responded that Robert was reported to be "very tired," which could have been from myocarditis. Tr. 87.

In Dr. Waters' opinion, Dr. Folkerth's statement that lymphocytic myocarditis and hypersensitivity or eosinophilic myocarditis are totally different illnesses is "solely a pathologist's perspective." Pet. Ex. 13 at 6. "From a pathologist's perspective[,] eosinophilic myocarditis has a mixed infiltrate with a significant percentage of eosinophils, rather than the requirement that it is primarily eosinophils." *Id*. at 7. Clinically, any type of myocarditis can cause sudden death. *Id*. at 6. Dr. Folkerth "relies on the most common epidemiologic cause of lymphocytic myocarditis," viral infection, but there is no evidence in this case of a viral illness within two weeks of the vaccination and "no support either clinically or in the autopsy for this contention." *Id*. at 7. Dr. Waters agreed with Dr. Folkerth that lymphocytic myocarditis is commonly attributed to viral infection and the causal virus is rarely identified. Tr. 145. However, in Dr. Waters' opinion, the lack of eosinophils on autopsy does not rule out a hypersensitivity response to the Menactra vaccine. Tr. 145-46.

B. Respondent's Experts

1. Dr. Scott Yeager

i. Qualifications

Dr. Scott Yeager received a Bachelor of Arts from Dartmouth College and a medical degree from the University of Virginia. Resp. Ex. B at 1. He completed a residency in pediatrics at the Medical Center Hospital of Vermont and a fellowship in cardiology at the Children's Hospital

Medical Center in Boston, MA. *Id*. He is board certified in pediatric and pediatric cardiology. *Id*. at 2. Since 1985, Dr. Yeager has served as the Division Chief of Pediatric Cardiology at the University of Vermont, where he was promoted to Professor of Pediatrics in 2012. *Id*. Dr. Yeager has been involved in teaching, clinical research, and the practice of pediatric cardiology for over 30 years. Resp. Ex. A at 1. According to Dr. Yeager, he spends about 20 percent of his time on teaching and clinical research. Tr. 153. The majority of his time, about 60 percent, is spent on his pediatric cardiology practice; he sees between 15 and 20 patients per week, and between two and six cases of myocarditis per year. Tr. 154. He also is the president and co-founder of the New England Congenital Cardiology Research Foundation and co-founder of the New England Congenital Cardiology Association. Resp. Ex. A at 1.

ii. Causation Opinion

Dr. Yeager opined that nothing in the medical literature supports Dr. Waters' theory that Menactra vaccine produces T-lymphocytes that can gravitate to the cardiac conduction system, causing lymphocytic myocarditis. Tr. 162-63; Resp. Ex. E at 1. In Dr. Yeager's opinion, Robert died from lymphocytic myocarditis caused by a viral infection.

Dr. Yeager testified that "about 10 percent of unexpected cardiac death is associated with myocarditis… It's a well recognized cause of sudden death." Tr. 175-76; Resp. Ex. A at 2-3; Resp. Ex. A, Tab 1 at 2.[45] Causes of myocarditis are variable and include 30 or more viruses, as well as bacteria, parasites, fungi, and toxins; hypersensitivity myocarditis specifically can be caused by drug reactions. Tr. 172. However, lymphocytic myocarditis is "almost exclusively caused by viruses." Tr. 176. Histologically, viral myocarditis is characterized by leukocyte infiltration, specifically lymphocytes and macrophages, as well as evidence of myocardial injury or fibrosis. Resp. Ex. A at 3; Resp. Ex. A, Tab 3 at 2;[46] Resp. Ex. A, Tab 6 at 2.[47] In his opinion as a clinician, 90 to 95% of myocarditis cases are lymphocytic. Tr. 159-60.

Dr. Yeager stated that patients with myocarditis can have variable presentations; some have "relatively minor" symptoms, like mild chest pain, while others exhibit profound fatigue, shortness of breath, and evidence of heart failure. Tr. 154-55. Many patients "are relatively well" but have abnormalities on an EKG or elevated cardiac enzymes indicative of myocarditis. Tr. 154. The vast majority of patients with myocarditis recover. Tr. 155. Biopsies of the heart are the gold standard, but due to the associated risk, they are not typically done unless the doctors suspect the patient has "some sort of exotic infection." Tr. 156-57. Dr. Yeager does not see patients who are asymptomatic because they do not show up in a clinical setting, but based on literature, he suspects that more than 50% of people with myocarditis do not have any symptoms and that viruses affect the heart more than is realized. Tr. 160-61. As an example, Dr. Yeager offered a study of 427 nontraumatic,

[45] Christian van der Werf et al., *Sudden Death in the Young: What Do We Know About It and How to Prevent?*, 3 CIRC. ARRHYTHM. ELECTROPHYSIOL. 96-104 (2010), filed as "Resp. Ex. A, Tab 1."

[46] Jared W. Magnani & G. William Dec, *Myocarditis: Current Trends in Diagnosis and Treatment*, 113 CIRCULATION 876-90 (2006), filed as "Resp. Ex. A, Tab 3."

[47] Heiko Mahrholdt et al., *Presentation, Patterns of Myocardial Damage, and Clinical Course of Viral Myocarditis*, 114 CIRCULATION 1581-90 (2006), filed as "Resp. Ex. A, Tab 6."

sudden deaths in people between the ages of 5 and 35. 11.6% of deaths were attributed to myocarditis; half of the subjects who died of myocarditis reported a "flu-like illness." Resp. Ex. A, Tab 13 at 3.[48] He stated therefore, "there is poor correlation between systemic viral symptoms and myocardial involvement in lymphocytic myocarditis." Resp. Ex. A at 3.

Dr. Yeager acknowledged that vaccines, like drugs, can cause hypersensitivity myocarditis, which is "characterized histologically primarily by eosinophilic infiltration." Resp. Ex. A at 3; *see also* Resp. Ex. A, Tab 7 at 9.[49] Dr. Yeager agreed that the smallpox vaccine can cause hypersensitivity myocarditis but stated that he was unaware of any other vaccines that could cause myocarditis. Tr. 166, 172, 175. To Dr. Yeager's knowledge, the smallpox vaccine activates a hypersensitivity reaction, resulting in eosinophilic infiltration; it is usually transient, and most patients recover. Tr. 175. Dr. Yeager stated that a biological mechanism would need to be provided in order for him to think that a particular vaccine could cause myocarditis. Tr. 170. When asked whether a hypersensitivity reaction could cause sudden death, Dr. Yeager stated, "I think it probably could…we probably don't have enough hypersensitivity myocarditis to actually do a study of [whether it is more or less] lethal than lymphocytic, but anything that causes inflammation and infiltration in heart muscle can set up a fatal arrhythmia." Tr. 176. When asked about the pathology of a Type IV hypersensitivity reaction, Dr. Yeager deferred to the pathologists. Tr. 173-74.

In his report, Dr. Yeager noted that there are "numerous reports of post-vaccination myocarditis associated with vaccines, particularly with small pox vaccination." Resp. Ex. A at 3; Resp. Ex. A, Tab 8.[50] Dr. Yeager submitted three case reports illustrating myocarditis associated with vaccines. In Boccara, the patient developed clinical signs of hypersensitivity myocarditis four days after receiving diphtheria, tetanus, and polio vaccinations; he was negative for viral infection and a biopsy did not show any inflammatory infiltrate. Resp. Ex. A, Tab 9 at 1-2.[51] The patient was treated with aspirin and released within 24 hours. *Id*. at 2. In Dilber, the patient developed clinical signs of hypersensitivity myocarditis three days after receiving a tetanus vaccination; the "patient's course was uneventful, and he was discharged on hospital day 4." Resp. Ex. A, Tab 10 at 1-2.[52] No biopsy was conducted; the type of cardiac infiltrate was not identified. In Thanjan, the case report discussed by Dr. Chang, *see supra* at 17, the patient developed clinical signs of hypersensitivity myocarditis two days after receiving DTaP, meningococcal conjugate, and

[48] Rajesh Puranik et al., *Sudden Death in the Young*, 2 HEART RHYTHM 1277-82 (2005), filed as "Resp. Ex. A, Tab 13."

[49] J. Butany et al., *Drug-related Cardiac Pathology*, 62 J. CLIN. PATHOL. 1074-84 (2009), filed as "Resp. Ex. A, Tab 7."

[50] Dimitri C. Cassimatis et al., *Smallpox Vaccination and Myopericarditis: A Clinical Review*, 43 J. AM. COLL. CARDIOL. 1503-10 (2004), filed as "Resp. Ex. A, Tab 8."

[51] Franck Boccara et al., *Acute Myopericarditis After Diphtheria, Tetanus, and Polio Vaccination*, 120 CHEST 671-72 (2001), filed as "Resp. Ex. A, Tab 9."

[52] Embiya Dilber et al., *Acute Myocarditis Associated with Tetanus Vaccination*, 78 MAYO CLIN. PROC. 1431-33 (2003), filed as "Resp. Ex. A, Tab 10."

hepatitis A vaccinations. Resp. Ex. A, Tab 11 at 1.[53] The patient was negative for viral infection. *Id*. at 1-2. He was released four days later on an anti-inflammatory drug. *Id*. No biopsy was performed, and the type of cardiac infiltrate not determined.

In Dr. Yeager's opinion, Dr. Waters' theory that the Menactra vaccine produced T-lymphocytes that gravitated to the cardiac conduction system and caused Robert's lymphocytic myocarditis is "a concept of post-vaccination myocarditis that was unfamiliar" to him. Resp. Ex. E at 1. Dr. Yeager explained, "…my understanding of the cardiac pathology is going to be based on reading scientific papers by pathologists and reading textbooks by pathologists, and I have never encountered that particular concept as a source of myocardial infiltration…. I'm not aware of such a mechanism." Tr. 162-63. In Dr. Yeager's opinion "hypersensitivity myocarditis is the generally recognized mechanism for vaccine related myocardial infiltration, and the histology in this case does not support that diagnosis." Resp. Ex. E at 1.

Dr. Yeager's review of the literature found only the two case reports filed by petitioner regarding meningococcal vaccine and myocarditis, Ball and Barton. Tr. 165. He emphasized that both patients discussed in Barton had eosinophilic infiltration on biopsy. Resp. Ex. A at 3; Resp. Ex. A, Tab 12 at 2-3. Overall, as a clinician, Dr. Yeager does not find case reports to be very helpful because it is one report out of "hundreds of millions of vaccines given." Tr. 181-82. The number of doses of a particular vaccine administered will dictate whether you see a rare event, because "you're going to find pretty rare events when you're talking that kind of volume," and meningococcal vaccine has had tens of millions, if not hundreds of millions, of doses administered. Tr. 169. "If meningococcal vaccination caused myocarditis with any measurable frequency, it would have become apparent beyond a single case report." Resp. Ex. E at 2.

When asked about Dr. Chang's opinion that Robert suffered from acute hypersensitivity myocarditis, Dr. Yeager responded that it "wasn't consistent with any pathologic model that has ever been presented to me either in texts or in scientific papers." Tr. 163.

In response to Dr. Chang's opinion that Robert's peripheral eosinophil level of 9.4% on the day of the vaccination supported a generalized hypersensitivity reaction, Dr. Yeager stated that, because the blood specimen was collected on the day of the vaccination, the elevated eosinophil level could not be ascribed to the vaccine. Resp. Ex. E at 2. Robert had elevated peripheral eosinophil levels in the past and was taking anti-convulsant medications, one of the most common causes of peripheral eosinophilia. *Id*. He added a patient can have eosinophilic infiltrate in the heart but a normal peripheral eosinophil level, or conversely, an elevated peripheral eosinophil level with nothing in the myocardium.[54] There is a weak correlation, if any, between elevated peripheral eosinophil level and myocarditis. Tr. 165.

---

[53] *See supra* n.32.

[54] In Barton, Patient One had eosinophilic infiltrate on biopsy but no peripheral eosinophilia, while Patient Two had eosinophilic infiltrate on biopsy with mild peripheral eosinophilia. Pet. Ex. 17 at 2-3; Resp. Ex. A, Tab 12 at 2-3. In Boccara, Dilber, and Thanjan, the patients all had clinical signs of hypersensitivity myocarditis but had peripheral eosinophil levels of 2.9, 3.0, and 3.7, respectively, all within the normal range. *See* Resp. Ex. A, Tab 9 at 1; Resp. Ex. A, Tab 10 at 2; Resp. Ex. A, Tab 11 at 1.

Dr. Yeager pointed out that Dr. Chang did not provide any literature to support his opinion that the absence of eosinophilic infiltrate on autopsy does not preclude a diagnosis of hypersensitivity myocarditis, an opinion that is "in conflict with the pathologic definition." Resp. Ex. E at 2. Dr. Yeager further pointed out that initially Dr. Waters did not "classify this case as a hypersensitivity myocarditis, but rather as some sort of myocardial infiltration by the vaccine-stimulated T cells. The petitioner's experts appear to be arguing conflicting pathologic mechanisms." *Id.*

Based on the statistics on myocarditis and sudden death, Dr. Yeager did not find anything about Robert's lack of symptoms or the sudden nature of his death to be inconsistent with what is seen in otherwise healthy young adults. Tr. 176. On autopsy, Robert's heart had "lymphocytic inflammatory infiltrate with focal myocyte necrosis." Resp. Ex. A at 2. There was no mention of eosinophils, and Robert's cause of death was determined to be lymphocytic myocarditis. *Id*. Moreover, "[c]ardiac microscopy showed patchy lymphocytic infiltration, the characteristic histologic findings of viral myocarditis…." *Id*. at 4. Dr. Yeager explained that "demonstrable involvement is often patchy, as demonstrated by this case, where only one of five sampled regions revealed active cellular infiltration." *Id*. at 3. Due to sampling errors, more than 17 samples would be necessary to correctly diagnose myocarditis in greater than 80% of cases. *Id*.; Resp. Ex. A, Tab 3 at 1;[55] Resp. Ex. A, Tab 2.[56] At hearing, Dr. Yeager was asked about the number of samples needed "to accurately get a pathology on the heart." Tr. 177. He explained that a larger number of samples is needed to rule out inflammation anywhere; he added that he was unaware of any circumstance where samples would show eosinophils in one part of the heart and lymphocytes in another.[57] Tr. 177-78. Dr. Yeager postured that "[e]osinophilic infiltration, which would be required for a diagnosis of hypersensitivity or drug-related myocarditis, was not observed" on Robert's autopsy. Resp. Ex. A at 4.

Dr. Yeager agreed with the medical examiner that Robert had lymphocytic myocarditis but conceded that he did not look at the slides because in death cases, he relies on the interpretation of the pathologist to help him understand the underlying cause. Tr. 157-59. However, he is familiar

[55] *See supra* n.46.

[56] The authors conducted a histopathologic review of 38 cases of lymphocytic myocarditis and found that, because lymphocytic myocarditis is generally mild, spotty, and uneven in distribution, it requires more than the three to five samples recommended by the Dallas criteria. Resp. Ex. A, Tab 2 at 1, 9. The authors further noted that lymphocytic myocarditis requires more samples than eosinophilic, giant cell, and granulomatous myocarditis because the normal myocardial interstitium contains a few lymphocytes but does not contain any of the other cell types. *Id*. at 10. Arthur J. Hauck et al., *Evaluation of Postmortem Endomyocardial Biopsy Specimens From 38 Patients With Lymphocytic Myocarditis: Implications for Role of Sampling Error*, 64 MAYO CLIN. PROC. 1235-45 (1989), filed as "Resp. Ex. A, Tab 2."

[57] Dr. Folkerth was put back on the stand to clarify the number of samples necessary for a histopathological diagnosis of myocarditis. Tr. 183. She explained that the articles referred to the number of samples required in a living patient; samples taken from a live person are much smaller than samples taken in an autopsy. Tr. 183. In this case, the five samples taken were "quite generous whole blocks of tissue, so you're looking at a lot more volume of tissue than you would see in biopsies." Tr. 183. If there were eosinophils in the heart on the autopsy in this case, they would have been picked up by the block samples taken. Tr. 183-84.

with the pathology of different types of myocarditis; because pathology showing eosinophils would lead to a different course of treatment than pathology showing lymphocytes. Tr. 158-59.

Ultimately, Dr. Yeager opined that Robert died from an "almost certainly viral" lymphocytic myocarditis which triggered a malignant ventricular arrhythmia. Resp. Ex. A at 4; Resp. Ex. E at 3. His Menactra vaccination was "entirely unrelated" and did not contribute to his myocarditis or sudden death "in any significant way." Resp. Ex. A at 4; Resp. Ex. E at 3.

2. Dr. Rebecca Folkerth

i. Qualifications

Dr. Rebecca Folkerth holds a Bachelor of Science from Indiana University and a medical degree from the University of Louisville School of Medicine. Resp. Ex. D at 1. She completed a residency in anatomic pathology at New England Medical Center and did fellowships in pathology and neuropathology at Harvard Medical School and Boston Children's Hospital, respectively. *Id*.

Dr. Folkerth began working as a pathologist at Brigham and Women's Hospital in 1991, focusing on surgical pathology and neuropathology. Resp. Ex. D at 2. In 2009, she became the director of the neuropathology division and began running the neuropathology training program for not only Brigham and Women's Hospital, but also Boston Children's Hospital and Beth Israel-Deaconess Medical Center. *Id*. at 3. Dr. Folkerth has also served as an associate professor of pathology at Harvard Medical School, a consultant in pathology at Boston Children's Hospital, and a consultant in medical oncology at Dana-Farber Cancer Institute. *Id*. at 2.

Dr. Folkerth is currently a pathologist with the Chief Medical Examiner's Office of New York, where she primarily focuses on forensic neuropathology. Tr. 90. Her office does about 5,000 autopsies a year. Tr. 91. She autopsies the brain and nervous system for about 700 to 900 cases per year. Tr. 91. Dr. Folkerth admitted that she is not board certified in pediatric pathology but after 28 years at Boston Children's Hospital and her current position, which involves numerous autopsies on children, she has significant experience in performing autopsies on children. Tr. 92. She has been practicing for over 25 years, has performed hundreds of postmortem examinations of adults, infants, and children, and has written over 100 peer reviewed articles and over 15 chapters for medical textbooks dealing with neuropathology. Resp. Ex. C at 2.

Dr. Folkerth has performed over 1,000 autopsies and spent 12 years as a surgical pathologist looking at endomyocardial biopsies. Tr. 120. She has written reports where myocarditis was the cause of death and has seen cases of myocarditis in the past year with the medical examiner's office. Tr. 120. She conceded that she could not recall the types of myocarditis identified in those cases. Tr. 120. She has never personally performed an autopsy where a vaccine was identified as the cause of death. Tr. 120. She admitted she does not know what VAERS, the CISA network, PRISM, or Vaccine Safety Datalink are and added that she is not an epidemiologist and does not know what a self-controlled study is. Tr. 121.

ii. Causation Opinion

Dr. Folkerth opined that Robert died from lymphocytic myocarditis, a condition known to cause sudden death. Resp. Ex. C at 4. In her opinion, there was no evidence that the Menactra vaccine played any causal role in Robert's death. *Id*. at 5-6.

She explained that "Myocarditis is defined as inflammation in the myocardium, accompanied by evidence of cell death of the cells that make up the myocardium…." Tr. 94-95. The heart is surrounded by a membrane and an outer layer of cells called the epicardium, with a layer of epicardial fat on the outside of the heart. Tr. 139.

Dr. Folkerth stated that her approach to examining myocarditis cases, which relies primarily on histopathology, is consistent with the approach favored by the general scientific community. Tr. 96-97. In her experience, and based on the literature, vaccine-associated myocarditis has eosinophilic inflammation. Tr. 97. Dr. Chang's suggestion that inflammation is inflammation and the infiltrate does not matter is simplistic; the type of infiltrate identified indicates different mechanisms. Tr. 97. Histopathologically, the infiltrate would consist of lymphocytes, eosinophils, histiocytes, or granulomatous cells. Tr. 116.

"A lymphocyte is a type of inflammatory cell. There are multiple types of inflammatory cells that the body produces, and each one is called to action in certain specific settings." Tr. 93. Lymphocytes are a marker of chronic inflammation. Tr. 140. On a slide, a lymphocyte looks like a small, blue, round cell. Tr. 93. Eosinophils have a "very distinctive appearance…completely different from lymphocytes…. So it's quite easy to tell them apart on a slide or even in peripheral blood." Tr. 93-94. "There's no way you would confuse an eosinophilic infiltrate with a lymphocytic infiltrate." Tr. 96. Though there may be mixed infiltrates, the "presence of eosinophils at all would lead you to a sensitivity, and the hypersensitivity or allergic type [of myocarditis]. And the absence of eosinophils would lead you away from that diagnosis." Tr. 96; Resp. Ex. F at 1 ("[E]osinophilic refers to the type of inflammatory cell associated with hypersensitivity (allergic type) reactions…whereas lymphocytic refers to inflammation almost certainly related…to viral infection.") (emphasis omitted).

Dr. Folkerth explained that the pattern of inflammation on Robert's heart and the presence of lymphocytes is evidence of viral myocarditis. Tr. 108-09. The most common cause of lymphocytic myocarditis is viral infection, which was most likely the cause of death in this case, "even though studies to detect the most common viruses (Coxsackie [enterovirus], adenovirus, herpes virus type 6, or parvovirus B19) were not available." Resp. Ex. C at 5. Dr. Folkerth noted that, if the paraffin blocks containing the tissue samples still exist, they could be sent to the CDC for viral testing.[58] Tr. 142. However, "the inability to identify a particular virus is the usual clinical situation and does NOT (sic) decrease the likelihood" that a virus caused Robert's lymphocytic myocarditis. Resp. Ex. F at 1; Tr. 100-01, 107-08. "[I]t's the usual situation that someone can be infected and not know it and have a sudden cardiac death." Tr. 109. She agreed with the autopsy report's conclusion that Robert suffered from lymphocytic myocarditis based on the presence of lymphocytic inflammation in the myocardium. Tr. 98. "It's pretty clear-cut what happened here. I think it was the viral myocarditis, and it was fatal, and it was asymptomatic, as they often are." Tr. 112. She further noted that the heart tissue showed inflammation in the epicardial fat; in Dr. Folkerth's opinion, this is a marker for the degree of the severity of inflammation. Tr. 139-140.

[58] Petitioner filed a status report on April 2, 2018, advising that the paraffin blocks no longer exist.

"That type of inflammation takes some days to weeks to develop. That's not an acute type of reaction." Tr. 140.

In her report, Dr. Folkerth stated, "While one cannot absolutely exclude the possibility that Robert succumbed to an immunologic reaction related to vaccination, this is not likely given the much higher prevalence of viral myocarditis and its known propensity to precipitate sudden death." Resp. Ex. C at 5. Epidemiology favors lymphocytic myocarditis rather than an unrelated single second dose of vaccination Robert received three days prior to his death. *Id*. When asked about this statement at hearing, Dr. Folkerth stated that "anything is possible," but a reaction to a Menactra vaccine would not be consistent with the pattern of inflammation seen on autopsy in this case. Tr. 117-19. In an experimental animal model, you could "give it a vaccine and cause this…it's possible, but I wouldn't call it biologically plausible." Tr. 119. Based on all of the evidence available, the most likely series of events is that Robert developed lymphocytic myocarditis caused by a virus. Tr. 117.

Dr. Folkerth explained that "the Menactra vaccine is generated from some of the sugars that are on the outside capsule of the meningococcus bacterium," and those sugars are then stuck to a separate unrelated protein. Tr. 113. When the vaccine is injected, it "causes the body to develop lymphocytes that will then recognize that combination of sugars as being meningococcus. So then if the person is later exposed to meningococcus, the T-cells will go and kill the bacterium…." Tr. 113.

Dr. Folkerth agreed that T-lymphocytes would be produced as a typical immune response to the Menactra vaccine or any other "offending organism" including actual meningococcal bacteria. Tr. 135-37. However, there is no pathophysiological support for Dr. Waters' opinion that the T-lymphocytes produced in response to the Menactra vaccine gravitated to the heart or that the vaccine is analogous to actual live meningococcal bacteria. Tr. 112.

Dr. Folkerth agreed with Dr. Waters' explanation of Type I and Type IV hypersensitivity reactions. Tr. 125. However, Dr. Folkerth added that an analysis of Type I vs. Type IV hypersensitivity is an immunologic textbook type of explanation that is not practical in terms of histopathology and is not the terminology used on a daily basis when examining tissue. Tr. 100. A practical analysis focuses on whether the type of cell present is an eosinophil, lymphocyte, or histiocytic granuloma. Tr. 100.

Dr. Folkerth also agreed that a person could have simultaneous Type I and Type IV reactions but did not agree with Dr. Waters that one could have a Type I reaction and later a Type IV reaction. Tr. 125-26. Dr. Folkerth agreed with Dr. Waters that, in order to prove this was possible, a patient would have to undergo constant endomyocardial biopsies over several weeks, which would be unethical. Tr. 125-26. Dr. Folkerth disagreed with Dr. Waters' suggestion that there were eosinophils first that disappeared, leaving only lymphocytes; proving that would also require several biopsies, and is not consistent with the literature on Type I and Type IV reactions. Tr. 126. Dr. Folkerth agreed that a hypersensitivity myocarditis could have the presence of lymphocytes with eosinophils but not lymphocytes alone. Tr. 99-100.

Dr. Folkerth further agreed that Menactra could cause an allergic reaction, hypersensitivity response, or eosinophilic response in a sensitive person. Tr. 128-31. An acute hypersensitivity response, like an asthma attack, can take minutes to hours. Tr. 131-32. A hypersensitivity response that takes days would be a Type IV response. Tr. 132. Dr. Folkerth admitted that she did not know how long it would take for eosinophils to be seen in the heart following a Type I hypersensitivity response but noted that eosinophils can be seen in tissue relatively quickly after exposure. Tr. 132-34. For example, eosinophils can be seen in the trachea tissue of a person who dies from an asthma attack, even though the death would occur less than an hour after exposure. Tr. 132-33.

When asked whether it was possible to see an elevated level of eosinophils in peripheral blood after receiving a Menactra vaccination, Dr. Folkerth admitted that she did not know. Tr. 126-27. However, Dr. Folkerth explained, Robert's elevated peripheral eosinophil level of 9.4% is not very helpful because "unless you had a blood draw taken before he received the vaccine, showing that it was below nine, there's no way you can say that the vaccine caused it to go up. He could have had that eosinophil count walking into the doctor's office and very likely did."[59] Tr. 127. She noted that Robert's previous eosinophil level was six, which is "on the high side" of normal; he was also on "medications that are known to cause peripheral eosinophilia…." Tr. 127-28. Dr. Folkerth added, "you can have an eosinophilic infiltrate in tissue and have a normal blood eosinophil count and vice versa. They are not necessarily correlated." Tr. 128. When asked why she did not mention Robert's antiseizure medication as a possible cause of his myocarditis, Dr. Folkerth explained that, if the medications had caused a hypersensitivity response, Robert would have had eosinophilic infiltrate in the heart instead of lymphocytic infiltrate. Tr. 113.

In response to Dr. Chang's opinion that Robert suffered from hypersensitivity myocarditis, Dr. Folkerth cited to several articles which describe the characteristics of different types of myocarditis, specifically distinguishing hypersensitivity myocarditis from lymphocytic myocarditis. Resp. Ex. C at 5; Resp. Ex. C, Tab 1 at 1 ("Numerous medications…can induce hypersensitivity eosinophilic myocarditis, which commonly is reversible after withdrawal of the causative agent");[60] Resp. Ex. C, Tab 2 at 5 (Characterizing myocarditis associated with drugs or vaccines as "hypersensitivity eosinophilic myocarditis");[61] Resp. Ex. C, Tab 3 at 1 ("In general, the histologic patterns of myocarditis are categorized by the predominant inflammatory cells and can be divided into lymphocytic (including viral and autoimmune forms)…eosinophilic (hypersensitivity myocarditis or hypereosinophilic syndrome….").[62] Dr. Folkerth also rejected Dr. Chang's comparison of this case to the patient in Thanjan.[63] Resp. Ex. C at 5. Dr. Folkerth pointed

[59] It was never established whether Robert's blood work was done before or after he received the Menactra vaccine. Petitioner's experts made assumptions without evidence in the record. However, the literature does not support a correlation between peripheral eosinophils and eosinophilic infiltrate in the tissue.

[60] Ingrid Kindermann et al., *Update on Myocarditis*, 59 J. AM. COLL. CARDIOL. 779-92 (2012), filed as "Resp. Ex. C, Tab 1."

[61] Sandeep Sagar et al., *Myocarditis*, 379 LANCET 738-47 (2011), filed as "Resp. Ex. C, Tab 2."

[62] Ayelet Shauer et al., *Acute Viral Myocarditis: Current Concepts in Diagnosis and Treatment*, 15 ISR. MED. ASSOC. J. 180-85 (2013), filed as "Resp. Ex. C, Tab 3."

[63] *See supra* n.32.

out that the adolescent in Thanjan received multiple vaccinations, developed arthralgia and chest pain, and was diagnosed with hypersensitivity myocarditis based on elevated cardiac enzymes, abnormal ECG, and negative viral studies. *Id*. Notably, the patient in Thanjan did not undergo endomyocardial biopsy. *Id*. After the hearing, Dr. Folkerth responded to the Yamamoto case report submitted by petitioner, stating that it was not relevant to this matter because Yamamoto dealt with biopsy-proven eosinophilic myocarditis following a tetanus vaccination. Resp. Ex. F; Pet. Ex. 28. She added that eosinophilic myocarditis is a completely different type of heart inflammation than lymphocytic myocarditis, which is what Robert had.

V. Applicable Law

A. Legal Standard Regarding Causation

The Vaccine Act provides two avenues for petitioners to receive compensation. First, a petitioner may demonstrate a "Table" injury—i.e., an injury listed on the Vaccine Injury Table that occurred within the provided time period. § 11(c)(1)(C)(i). "In such a case, causation is presumed." *Capizzano v. Sec'y of Health & Human Servs.*, 440 F.3d 1317, 1320 (Fed. Cir. 2006); *see* § 13(a)(1)(B). Second, where the alleged injury is not listed on the Vaccine Injury Table, a petitioner may demonstrate an "off-Table" injury, which requires that the petitioner "prove by a preponderance of the evidence that the vaccine at issue caused the injury." *Capizzano*, 440 F.3d at 1320; *see* § 11(c)(1)(C)(ii). Initially, a petitioner must provide evidence that he or she suffered, or continues to suffer, from a definitive injury. *Broekelschen v. Sec'y of Health & Human Servs*., 618 F.3d 1339, 1346 (Fed. Cir. 2010). A petitioner need not show that the vaccination was the sole cause, or even the predominant cause, of the alleged injury; showing that the vaccination was a "substantial factor" and a "but for" cause of the injury is sufficient for recovery. *See Pafford v. Sec'y of Health & Human Servs.*, 451 F.3d 1352, 1355 (Fed. Cir. 2006); *Shyface v. Sec'y of Health & Human Servs.*, 165 F.3d 1344, 1352 (Fed. Cir. 1999).[64]

To prove causation for an "off-Table" injury, petitioners must satisfy the three-pronged test established in *Althen v. Sec'y of Health & Human Servs*., 418 F.3d 1274 (Fed. Cir. 2005). *Althen* requires that petitioners show by preponderant evidence that a vaccination petitioner received caused his or her injury "by providing: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." *Id*. at 1278. Together, these prongs must show "that the vaccine was 'not only a but-for cause of the injury but also a substantial factor in bringing about the injury.'" *Stone v. Sec'y of Health & Human Servs*., 676 F.3d 1373, 1379 (Fed. Cir. 2012) (quoting *Shyface*, 165 F.3d at 1352-53). Causation is determined on a case-by-case basis, with "no hard and fast per se scientific or medical rules." *Knudsen v. Sec'y of Health & Human Servs*., 35 F.3d 543, 548 (Fed. Cir. 1994). Petitioners are not required to identify "specific biological mechanisms" to establish causation, nor are they required to present "epidemiologic studies, rechallenge, the presence of pathological

[64] The Vaccine Act also requires petitioners to show by preponderant evidence the vaccinee suffered from the "residual effects or complications" of the alleged vaccine-related injury for more than six months, died from the alleged vaccine-related injury, or required inpatient hospitalization and surgical intervention as a result of the alleged vaccine-related injury. § 11(c)(1)(D). It is undisputed that this requirement is satisfied in this case.

markers or genetic disposition, or general acceptance in the scientific or medical communities." *Capizzano*, 440 F.3d at 1325 (quoting *Althen*, 418 F.3d at 1280). "[C]lose calls regarding causation are resolved in favor of injured claimants." *Althen*, 418 F.3d at 1280.

Each of the *Althen* prongs requires a different showing. The first *Althen* prong requires petitioner to provide a "reputable medical theory" demonstrating that the vaccines received *can* cause the type of injury alleged. *Pafford*, 451 F.3d at 1355-56 (citation omitted). To satisfy this prong, petitioner's "theory of causation must be supported by a 'reputable medical or scientific explanation.'" *Andreu ex rel. Andreu v. Sec'y of Health & Human Servs.*, 569 F.3d 1367, 1379 (Fed. Cir. 2009) (quoting *Althen*, 418 F.3d at 1278). This theory need only be "legally probable, not medically or scientifically certain." *Id.* at 1380 (emphasis omitted) (quoting *Knudsen*, 35 F.3d at 548). Nevertheless, "petitioners [must] proffer trustworthy testimony from experts who can find support for their theories in medical literature." *LaLonde v. Sec'y of Health & Human Servs.*, 746 F.3d 1334, 1341 (Fed. Cir. 2014).

The second *Althen* prong requires proof of a "logical sequence of cause and effect." *Capizzano*, 440 F.3d at 1326 (quoting *Althen*, 418 F.3d at 1278). In other words, even if the vaccinations can cause the injury, petitioner must show "that it did so in [this] particular case." *Hodges v. Sec'y of Health & Human Servs.*, 9 F.3d 958, 962 n.4 (Fed. Cir. 1993) (citation omitted). "A reputable medical or scientific explanation must support this logical sequence of cause and effect," *id.* at 961 (citation omitted), and "treating physicians are likely to be in the best position to determine whether a logical sequence of cause and effect show[s] that the vaccination was the reason for the injury," *Paluck v. Sec'y of Health & Human Servs.*, 786 F.3d 1373, 1385 (Fed. Cir. 2015) (quoting *Andreu*, 569 F.3d at 1375). Petitioner is not, however, required "to eliminate alternative causes as part of establishing [their] prima facie case." *Doe v. Sec'y of Health & Human Servs.*, 601 F.3d 1349, 1357-58 (Fed. Cir. 2010); *see Walther v. Sec'y of Health & Human Servs.*, 485 F.3d 1146, 1152 (Fed. Cir. 2007) (holding that a "petitioner does not bear the burden of eliminating alternative independent potential causes").

To satisfy the third *Althen* prong, petitioner must establish a "proximate temporal relationship" between the vaccination and the alleged injury. *Althen*, 418 F.3d at 1281. This "requires preponderant proof that the onset of symptoms occurred within a timeframe for which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation-in-fact." *De Bazan v. Sec'y of Health & Human Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). Typically, "a petitioner's failure to satisfy the proximate temporal relationship prong is due to the fact that onset was too late after the administration of a vaccine for the vaccine to be the cause." *Id.* However, "cases in which onset is too soon" also fail this prong; "in either case, the temporal relationship is not such that it is medically acceptable to conclude that the vaccination and the injury are causally linked." *Id.*; *see also Locane v. Sec'y of Health & Human Servs.*, 685 F.3d 1375, 1381 (Fed. Cir. 2012) ("[If] the illness was present before the vaccine was administered, logically, the vaccine could not have caused the illness.").

B. Legal Standard Regarding Fact Finding

The process for making factual determinations in Vaccine Program cases begins with analyzing the medical records, which are required to be filed with the petition. § 11(c)(2). Medical

records created contemporaneously with the events they describe are presumed to be accurate and "complete" such that they present all relevant information on a patient's health problems. *Cucuras v. Sec'y of Health & Human Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993). In making contemporaneous reports, "accuracy has an extra premium" given that the "proper treatment hang[s] in the balance." *Id.* Contemporaneous medical records that are clear, consistent, and complete warrant substantial weight "as trustworthy evidence." *Id*. Indeed, "where later testimony conflicts with earlier contemporaneous documents, courts generally give the contemporaneous documentation more weight." *Campbell ex rel. Campbell v. Sec'y of Health & Human Servs.*, 69 Fed. Cl. 775, 779 (2006); *see United States v. U.S. Gypsum Co.*, 333 U.S. 364, 396 (1948). But petitioners can support their claim with oral testimony if it is credible and consistent with the medical records. *See, e.g.*, *Stevenson ex rel. Stevenson v. Sec'y of Health & Human Servs.*, No. 90-2127V, 1994 WL 808592, at *7 (Fed. Cl. Spec. Mstr. June 27, 1994) (crediting the testimony of a fact witness whose "memory was sound" and "recollections were consistent with the other factual evidence"). In short, "the record as a whole" must be considered. § 13(a).

C. Evaluating Expert Testimony

Establishing a sound and reliable medical theory connecting the vaccine to the injury often requires a petitioner to present expert testimony in support of his or her claim. *Lampe v. Sec'y of Health & Human Servs.*, 219 F.3d 1357, 1361 (Fed. Cir. 2000). The Supreme Court's opinion in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993), requires that courts determine the reliability of an expert opinion before it may be considered as evidence. "In short, the requirement that an expert's testimony pertain to 'scientific knowledge' establishes a standard of evidentiary reliability." *Id*. at 590 (citation omitted). Thus, for Vaccine Act claims, a "special master is entitled to require some indicia of reliability to support the assertion of the expert witness." *Moberly ex rel. Moberly v. Sec'y of Health & Human Servs.*, 592 F.3d 1315, 1324 (Fed. Cir. 2010). The *Daubert* factors are used in the *weighing* of the reliability of scientific evidence proffered. *Davis v. Sec'y of Health & Human Servs.*, 94 Fed. Cl. 53, 66-67 (2010) ("uniquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted"). Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen*, 618 F.3d at 1347 (citing *Lampe*, 219 F.3d at 1362). And nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder ex rel. Snyder v. Sec'y of Health & Human Servs.*, 88 Fed. Cl. 706, 743 (2009) (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997)).

D. Consideration of Medical Literature

Finally, although this decision discusses some but not all of the literature in detail, the undersigned reviewed and considered all of the medical records and literature submitted in this matter. *See Moriarty ex rel. Moriarty v. Sec'y of Health & Human Servs.*, 844 F.3d 1322, 1328 (Fed. Cir. 2016) ("We generally presume that a special master considered the relevant record evidence even though [s]he does not explicitly reference such evidence in h[er] decision."); *Simanski v. Sec'y of Health & Human Servs.*, 115 Fed. Cl. 407, 436 (2014) ("[A] Special Master

is 'not required to discuss every piece of evidence or testimony in her decision.'" (citation omitted)), *aff'd*, 601 F. App'x 982 (Fed. Cir. 2015).

VI. Analysis

Because petitioner does not allege an injury listed on the Vaccine Injury Table, her claim is classified as "off-Table." As noted above, for petitioner to prevail on an "off-Table" claim, she must show by preponderant evidence that Robert's injury resulted from the vaccination at issue. *Capizzano*, 440 F.3d at 1320. Doing so shifts the burden to respondent to show that the injury was caused by factors unrelated to the vaccinations. *Deribeaux ex rel. Deribeaux v. Sec'y of Health & Human Servs.*, 717 F.3d 1363, 1367 (Fed. Cir. 2013).

A. Overview of Myocarditis

Myocarditis is an inflammation of the muscular walls of the heart. DORLAND'S at 1222. Myocarditis can be difficult to diagnose because it has a wide variety of causes and clinical presentations. Resp. Ex. A, Tab 3 at 1.[65] Myocarditis is classified into types based on histopathology. "Active myocarditis is characterized by an inflammatory cellular infiltrate with evidence of myocyte necrosis." *Id*. The inflammatory infiltrate can be described as lymphocytic, eosinophilic, or granulomatous. *Id*. "The amount of inflammation may be mild, moderate, or severe, and its distribution may be focal, confluent, or diffuse, respectively." *Id*.

Lymphocytic myocarditis accounts for the majority of myocarditis cases. Resp. Ex. A, Tab 5 at 1. Enteroviruses, specifically coxsackie group A and B, are traditionally the predominant viral cause, but myocarditis can be caused by a variety of viruses, including influenza A and B, adenovirus, Epstein-Barr virus, herpes viruses, cytomegalovirus, yellow fever, and retroviruses. Resp. Ex. A, Tab 3 at 1; Resp. Ex. A, Tab 5 at 3-4;[66] Resp. Ex. A, Tab 6 at 1;[67] Pet. Ex. 18 at 4.[68] Bacterial infections, including *Neisseria meningitidis*, beta-hemolytic streptococci, diphtheria, and *Borrelia burgdorferi*, have been implicated in bacterial myocarditis. Pet. Ex. 18 at 4. "Advances in molecular techniques have demonstrated the presence of viral genome in the myocardium of a significant percentage of patients presenting with unexplained dilated cardiomyopathy…." Resp. Ex. A, Tab 3 at 1. These "techniques have substantiated the long-held perception that viral infection plays a key role in the development of active myocarditis." *Id*. at 2. In addition to enterovirus, hepatitis C virus has been reported in Japanese patients and parvovirus B19 in German patients. *Id*.

The pathogenesis for lymphocytic myocarditis is believed to be direct myocardial invasion

[65] *See supra* n.46.

[66] Neil E. Bowles et al., *Detection of Viruses in Myocardial Tissues by Polymerase Chain Reaction: Evidence of Adenovirus as a Common Cause of Myocarditis in Children and Adults*, 42 J. AM. COLL. CARDIOL. 466-72 (2003), filed as "Resp. Ex. A, Tab 5."

[67] *See supra* n.47.

[68] *See supra* n.37.

by cardiotropic virus or other infectious agents which rapidly progresses to a second phase of immunologic activation. Resp. Ex. A, Tab 3 at 3. In the last phase, CD4+ activation prompts clonal expansion of B cells, resulting in further myocytolysis,[69] additional local inflammation, and production of circulating anti-heart antibodies. *Id*. All three mechanisms may interact within the same host; the predominant pathogenic mechanism may vary according to host defenses and the specific infectious agent. *Id*. at 3-4. Clinical manifestations can range from no symptoms at all to cardiogenic shock, but the majority of patients are asymptomatic. *Id*. at 4; Resp. Ex. A, Tab 4 at 3.[70]

Endomyocardial biopsy, or taking tissue samples of the heart, is the gold standard for diagnosing myocarditis. Resp. Ex. A, Tab 4 at 6. Autopsy sampling of the heart is more extensive.

Eosinophilic, or hypersensitivity, myocarditis is characterized by eosinophilic infiltration, the degree of which depends on the underlying condition and the degree and duration of eosinophilic exposure. Pet. Ex. 25 at 1.[71] Eosinophilic myocarditis is associated with hypersensitivity reactions, immune-mediated disorders, infections, cancer, vaccines, and numerous medications including antidepressants, antibiotics, and antipsychotics. *Id*. at 1, 7. One case of eosinophilic myocarditis following smallpox vaccine has been confirmed by endomyocardial biopsy. Resp. Ex. A, Tab 3 at 3. In a large number of cases, however, the underlying cause is unknown. Pet. Ex. 25 at 1. The clinical presentation can vary widely, ranging from nonspecific symptoms of fever, dyspnea, and chest pain to peripheral blood eosinophilia, sinus tachycardia, and rash, to an acute fulminant necrotizing myocarditis or chronic restrictive cardiomyopathy that rapidly results in cardiovascular deterioration and circulatory collapse. Pet. Ex. 25 at 1, 3-5; Resp. Ex. A, Tab 3 at 3.

Eosinophilic myocarditis is most often fatal and discovered on autopsy. Pet. Ex. 25 at 2. A poor correlation exists between the degree of myocardial inflammation or necrosis and the likelihood of arrhythmias or hemodynamic collapse. Resp. Ex. A, Tab 3 at 3.

In what appears to be the largest study of eosinophilic myocarditis based on a series of published cases, Brambatti et. al. noted that hypersensitivity was the most frequently reported presentation of eosinophilic myocarditis. Pet. Ex. 25 at 4. Drugs most frequently associated with hypersensitivity eosinophilic myocarditis were antibiotics, central nervous system agents, vaccines, antitubercular agents, and other agents. *Id*. at 7-8. No specific vaccines were noted. Cessation of the offending drug was thought to be the most effective treatment. *Id*. at 12. Pathological findings showed that, in hypersensitivity eosinophilic myocarditis, eosinophilic myocardial infiltrates range from mild to severe, but did not correlate with the incidence of death or the levels of peripheral eosinophilia. *Id*. Furthermore, eosinophilic myocarditis often has a fulminant presentation with abrupt impairment of left ventricle ejection fraction and high risk of

[69] Myocytolysis is the disintegration of muscle fibers. *Myocytolysis*, DORLAND'S at 1222.

[70] Laurent Andreoletti et al., *Viral Causes of Human Myocarditis*, 102 ARCH. CARDIOVASC. DIS. 559-68 (2009), filed as "Resp. Ex. A, Tab 4."

[71] *See supra* n.42.

malignant arrhythmias. *Id*.

B. The Menactra Vaccine

Meningococcal disease is caused by *Neisseria meningitidis* bacteria. Pet. Ex. 27 at 1.[72] It is a serious bacterial illness that can lead to meningitis,[73] bacterial pneumonia, or bacteremia. *Id*. The bacterium has an inner and outer membrane; the outer membrane is surrounded by a polysaccharide capsule. *Id*. Meningococcal strains are classified based on the structure of this polysaccharide capsule. *Id*. Thirteen strains have been identified, but "[a]lmost all invasive disease is caused by one of five serogroups: A, B, C, W, and Y." *Id*. at 1-2.

Menactra "contains *N. meningitidis* serogroup A, C, Y, and W-135 capsular polysaccharide antigens individually conjugated to diphtheria toxoid protein." Pet. Ex. 26 at 25. The polysaccharides and the protein are purified and detoxified. *Id*. No preservative or adjuvant is added during manufacture. *Id*.; Pet. Ex. 27 at 6 (Menactra "does not contain a preservative or an adjuvant"). "An advantage of conjugate vaccines is their ability to elicit immunologic memory. Meningococcal conjugate vaccines prime the immune system, and immunologic memory persists even in the absence of detectible bactericidal antibodies." Pet. Ex. 27 at 8.

C. Petitioner Has Not Carried Her Burden of Proof

The experts agreed that Robert had myocarditis which caused his death. The experts also agreed that Robert had no symptoms of any viral illness in the weeks preceding his death. The experts disagree on the cause of Robert's myocarditis. Petitioner's expert Dr. Chang opined that Robert had a hypersensitivity myocarditis caused by the Menactra vaccine which ultimately lead to cardiac collapse. Dr. Waters opined that that Menactra vaccine is a T-lymphocyte mediated vaccine and therefore, the vaccine caused lymphocytic myocarditis which resulted in Robert's cardiac collapse and death; he may have also had a hypersensitivity reaction. Respondent's experts, Drs. Yeager and Folkerth, opined that Robert had lymphocytic myocarditis caused by viral infection which often goes undetected, is asymptomatic, and can cause sudden death; the Menactra vaccine had nothing to do with it and was merely temporally associated, which is of no consequence. Nothing in the autopsy suggests that Robert had a hypersensitivity or allergic myocarditis, as no eosinophils were found in the heart.

The Luminex Virus Assay Panel was a source of contention in this case. Dr. Folkerth admitted that she mistakenly made a reference in her report to a Luminex Virus Assay Panel with negative results for the viruses tested. Petitioner argued vehemently at hearing, and again during a status conference thereafter, that Dr. Folkerth's testimony should be stricken in its entirety as a result of this mistake. However, it was only petitioner's experts, neither of whom admittedly ever looked for the actual test or results, who relied solely on Dr. Folkerth's report as a basis for their opinions that the vaccine caused Robert's lymphocytic myocarditis and ultimate death because no

[72] CENTERS FOR DISEASE CONTROL AND PREVENTION, EPIDEMIOLOGY AND PREVENTION OF VACCINE-PREVENTABLE DISEASES 231-46 (Jennifer Hamborksy et al. eds., 13th ed. 2015), filed as "Pet. Ex. 27."

[73] Meningitis is an inflammation of the meninges, the three membranes that envelope the brain and spinal cord. *Meningitis*, DORLAND'S at 1132; *meninges*, *id.*

viral infection was ever found. Pet. Ex. 13 at 5; Pet. Ex. 11 at 4.

1. The Preponderance of the Evidence Indicates that Robert Suffered from Lymphocytic Myocarditis

The Federal Circuit has determined that if there is a dispute as to the nature of a vaccinee's injury, the special master may opine on the nature of said injury. *Contreras v. Sec'y of Health & Human Servs*., 844 F.3d 1363, 1368 (Fed. Cir. 2017), citing *Hibbard v. Sec'y of Health & Human Servs*., 698 F.3d 1355, 1365 (Fed. Cir. 2012).

As discussed above, a key dispute in this matter is whether Robert suffered from lymphocytic or eosinophilic myocarditis. In her pre-hearing brief and at hearing, petitioner took the position that Robert suffered lymphocytic myocarditis; however, in her post-hearing brief, petitioner argued that Robert had eosinophilic myocarditis. *See* Pet. Ex. 13 at 7; Pet. Brief at 7; Pet. Post-Hearing Brief at 6. Respondent maintained throughout the pendency of this matter that Robert suffered from lymphocytic myocarditis. *See* Resp. Brief at 3; Resp. Post-Hearing Brief at 1-2. The autopsy found the cause of death to be lymphocytic myocarditis. Pet. Ex. 3 at 10.

Drs. Chang, Waters, Folkerth, and Yeager agreed that Robert's autopsy showed lymphocytic infiltrate in the heart tissue, histopathological evidence of lymphocytic myocarditis, and no evidence of eosinophilic infiltrate in the heart tissue. Tr. 69, 70, 98, 108-09, 113, 126, 157-59, 206, 208; Resp. Ex. A at 2, 4. Drs. Waters, Yeager, and Folkerth agreed that absence of eosinophils on biopsy would preclude a diagnosis of eosinophilic myocarditis. Tr. 99-100, 149-50; Resp. Ex. A at 4. Dr. Chang only commented on the relationship of eosinophilic infiltrate to hypersensitivity myocarditis, opining that hypersensitivity myocarditis could be characterized by either eosinophils or lymphocytes. Tr. 190-91, 194, 204-05, 224; Pet. Ex. 11 at 4. Dr. Yeager pointed out that Dr. Chang did not support this opinion with any literature. Resp. Ex. E at 2.

Petitioner submitted that, despite the lack of eosinophilic infiltrate in the heart, the elevated level of peripheral eosinophils is sufficient for a showing of eosinophilic myocarditis. *See* Pet. Post-Hearing Brief at 6. Both Dr. Chang and Dr. Waters pointed to the peripheral eosinophilia as evidence of a hypersensitivity reaction. Tr. 36, 51-52, 54, 192-93; Pet. Ex. 11 at 4. Drs. Yeager and Folkerth provided evidence that there is a weak correlation between peripheral eosinophilia and eosinophilic myocarditis. Tr. 128, 165. According to respondent's experts, a person can have eosinophilic myocarditis without elevated peripheral eosinophils, or elevated peripheral eosinophils without eosinophilic myocarditis. Tr. 128, 165. Literature submitted by respondent supports the lack of correlation. *See* Resp. Ex. A, Tab 12 at 3[74] ("…patients with eosinophilic myocarditis resulting from hypersensitivity have mildly elevated or normal eosinophil counts"); Resp. Ex. C, Tab 2 at 5[75] ("Hypersensitivity myocarditis is particularly difficult to recognize because the clinical features characteristic of a drug hypersensitivity reaction—including non-specific skin rash, malaise, fever, and eosinophilia—are absent in most cases"). Respondent's experts also noted that Robert's anti-seizure medications could have caused elevated peripheral eosinophil levels, *see* Tr. 141, 164, Resp. Ex. E at 2, including Robert's previously elevated

[74] *See supra* n.40.

[75] *See supra* n. 61.

peripheral eosinophil levels of 6.0 and 7.2 on January 23, 2012 and February 11, 2011, respectively. *See* Pet. Ex. 1 at 58; Pet. Ex. 2.2 at 21. Petitioner's experts agreed that Robert's anti-seizure medications could have contributed to his elevated eosinophil levels but opined that the medications would not have caused "an acute increase" on the same day that Robert received the Menactra vaccine. Tr. 60-61, 199. However, as Dr. Folkerth pointed out, the medical records do not indicate whether Robert's blood work was taken before or after he received the Menactra vaccine, so he could have arrived at Dr. Barsh's office with an elevated eosinophil level of 9.0. Tr. 127.

The literature submitted by both parties overwhelmingly supports endomyocardial biopsy as the "gold standard" in diagnosing myocarditis; essentially, the biopsy results are the determinative factor in whether a patient has myocarditis, and if so, the type of myocarditis. *See, e.g.*, Resp. Ex. A, Tab 3 at 5 ("EMB findings remain the gold standard for unequivocally establishing the diagnosis."); Resp. Ex. A, Tab 4 at 9 ("…the analysis of EMB is the gold standard for establishing the diagnosis unequivocally…"); Resp. Ex. C, Tab 1 at 1 ("Endomyocardial biopsy remains the gold standard for in vivo diagnosis of myocarditis."); Resp. Ex. C, Tab 2 at 6 ("Histological or immunohistological evidence of an inflammatory cell infiltrate with or without myocyte damage is the gold standard for the diagnosis of myocarditis").

Petitioner further submitted that, without evidence that Robert had a viral infection, the tissue samples showing lymphocytic infiltrate in the heart is insufficient for a diagnosis of lymphocytic myocarditis. Pet. Post-Hearing Brief at 4. It was established after lengthy discussion during the hearing that the Luminex Virus Assay Panel, which was purportedly negative for viral infection, was never conducted. Tr. 41-44, 101-06. Accordingly, it is unknown whether Robert was suffering from a viral infection at the time of his death. The experts agreed that lymphocytic myocarditis is most commonly caused by viruses. Tr. 47, 80, 99, 159-60, 176, 213; Pet. Ex. 13 at 6; Resp. Ex. A at 3; Resp. Ex. C at 5. However, Dr. Waters opined that Robert fell into the 50% of myocarditis cases that are not caused by viruses. Tr. 84. She could not however provide support for this statistic. Further, she stated, "I've heard that Robert was very tired" in the days following his vaccination, "and he could have been tired because he had some myocarditis," but could not explain why fatigue would not also be a symptom of a viral infection. Tr. 87.

The petitioner has the burden of proving, by a preponderance of the evidence, that the vaccinee actually suffered from the injury which they are alleging was caused by the vaccine. *See Hibbard*, 698 F.3d at 1365. The record is replete with support for the primacy of endomyocardial biopsy results in determining a diagnosis of myocarditis. Petitioner has not refuted this support, nor has she provided literature to support her argument that peripheral eosinophilia, absent eosinophilic infiltrate on biopsy, is sufficient for a diagnosis of eosinophilic myocarditis. Robert's heart tissue showed lymphocytic infiltrate alone. The autopsy concluded his death was from lymphocytic myocarditis. The opinion of a medical examiner is equivalent to that of a treating physician and should be afforded the same consideration. *Nordwall ex rel. Tori v. Sec'y of Health & Human Servs*., 83 Fed. Cl. 477, 488 (2008) ("An autopsy report by a medical examiner is without question a contemporaneous medical record"). Accordingly, I find that Robert suffered from lymphocytic, not eosinophilic, myocarditis.

2. *Althen* Analysis

i. *Althen* Prong One: Petitioner Has Failed to Proffer a Reputable Medical Theory that the Menactra Vaccine Can Cause Lymphocytic Myocarditis

Petitioner offered two theories in this case. The first based on a statement found in an article that "[M]eningococcal conjugate vaccines, through conjugation of polysaccharide to a protein carrier, change the immune response from T-cell independent to T-cell dependent, leading to improved immunogenicity over polysaccharide vaccines," which Dr. Waters stated meant that T-lymphocytes generated by the immune system in response to the Menactra vaccine "gravitated to the heart's conduction system causing a lethal arrhythmia and sudden death." Pet. Ex. 13 at 6-7, referencing Pet. Ex. 21 at 1. "The fact that we have a lymphocytic response is certainly very consistent with the cause being the vaccine and the time course is appropriate." Tr. 56-57. Dr. Waters provided no explanation for how the T-cell mediated immune response to the Menactra vaccine compares with the pathogenesis of lymphocytic myocarditis.

When asked if there was any literature which supported her opinion that Menactra vaccine could cause lymphocytic myocarditis, Dr. Waters stated that the package insert discussed the mechanism of action for the vaccine through T-lymphocytes. Tr. 78. "Moreover, the meningococcal vaccines are relatively new and have not been as widely distributed as smallpox or DTP which have both demonstrated vaccine-caused myocarditis." Pet. Ex. 13 at 7. To that end, Dr. Waters was asked to confirm that Barton, when discussing two cases of eosinophilic myocarditis following vaccination, had concluded that, if evidence existed for an association between myocarditis and meningococcal vaccine, it would be eosinophilic, not lymphocytic, myocarditis. Dr. Waters responded, "It suggests that in two out of their two cases the eosinophilic part was histologically seen." Tr. 77-78. Dr. Waters admitted that those were the two cases she referred to and based her report on.

Dr. Waters' theory that the meningococcal vaccine can cause lymphocytic myocarditis was premised on the body's intended response to the Menactra vaccine through T-cells in order to create immunity. Dr. Waters could point to nothing in the record to support the theory that this process or any vaccine including the meningococcal vaccine could cause lymphocytic myocarditis. Furthermore, Dr. Waters did not and could not provide any literature to support her opinion that lymphocytic myocarditis has been associated with drugs, toxins, or vaccines. All of the literature submitted in this matter by both petitioner and respondent unequivocally described lymphocytic myocarditis as an inflammation due to lymphocytes and macrophages commonly associated with viral syndrome, and eosinophilic myocarditis as associated with allergic or hypersensitivity reactions to drugs, toxins, vaccines, parasites, and cancer. Even in cases where mixed infiltrates were found, the presence of eosinophils was the determining factor in distinguishing lymphocytic myocarditis from eosinophilic myocarditis. Succinctly, Dr. Waters could not explain how the Menactra vaccine could cause lymphocytic myocarditis, nor could she point to any literature showing any association between vaccines and lymphocytic myocarditis.

Petitioner's second theory was that the Menactra vaccine can cause a hypersensitivity reaction resulting in lymphocytic myocarditis and cardiac death. Dr. Waters joined Dr. Chang on this theory. Dr. Waters opined that the Menactra vaccine can cause an anamnestic T-lymphocyte

cell response to the Menactra, which causes inflammation leading to a hypersensitivity response. Dr. Waters suggested that a Type IV hypersensitivity reaction only produces lymphocytes. Tr. 68-69, 83. However, Dr. Waters admitted that hypersensitivity myocarditis by definition is eosinophilic. Tr. 65. She hedged, "I think hypersensitivity myocarditis can present histologically as either lymphocytic myocarditis or eosinophilic myocarditis." Tr. 66. However, she was unable to point to any literature in the record that supported this proposition other than to say that Byard infers it, "but it's – as I mentioned before, hypersensitivity is more—is a clinical term." Tr. 66-67.

Dr. Chang maintained that the Menactra vaccine caused a hypersensitivity reaction, stating that an inflammatory process from vaccination could lead to either eosinophilic and/or lymphocytic myocarditis. However, when asked about the distinction made between lymphocytic myocarditis as viral and eosinophilic myocarditis as a hypersensitivity reaction, Dr. Chang submitted that it did not matter how the myocarditis was classified because clinically, patients do not always fit all of the criteria for certain classifications. Tr. 204-05. Further, Dr. Chang stated that the type of myocarditis did not matter to him because it would not change the way that he would treat the patient. Tr. 197, 218. Dr. Chang's responses in this case begs the question of why he was asked to serve as an expert in this case.

Dr. Folkerth testified that there is no pathophysiological support for Dr. Waters' theory. Although Menactra, like any other drug or vaccine, could cause an allergic reaction or hypersensitivity response in a sensitive person, such a response would be characterized by eosinophils. Tr. 128-31. A hypersensitivity myocarditis could have a mixed infiltrate with eosinophils and lymphocytes, but not lymphocytes alone. Tr. 99-100; *see also* Pet. Ex. 17 at 3 ("Clinically, hypersensitivity myocarditis is indistinguishable from myocarditis resulting from other causes. The nature of the inflammatory infiltrate present in myocardial tissue biopsy is a key for differentiating etiology… Thus, the finding of an eosinophilic infiltrate on myocardial biopsy in both our patients strongly suggests a hypersensitivity phenomenon, as opposed to a lymphocytic infiltrate, characteristic of viral etiology."); Resp. Ex. A, Tab 7 at 10[76] ("The presence of eosinophils in the myocardium-interstitium, at endomyocardial biopsy or at autopsy, should alert the pathologist to the possibility of a hypersensitivity myocarditis.").

Dr. Yeager testified that Dr. Waters' theory that Menactra vaccine produces T-lymphocytes that gravitate to the cardiac conduction system causing lymphocytic myocarditis cannot be found anywhere in the available medical literature. Tr. 162-63; Resp. Ex. E. He agreed that smallpox vaccine can activate a hypersensitivity reaction and eosinophilic infiltration but stated that he has not seen any scientific literature or texts that discuss vaccines causing a hypersensitivity reaction characterized by only lymphocytic infiltrate. Tr. 163-64, 172, 175. Dr. Yeager added he had run a recent review of the literature and could find nothing other than the case reports cited by petitioner regarding meningococcal vaccine and myocarditis. Tr. 165.

As for the case reports cited by petitioner, three out of four case reports discuss vaccines associated with eosinophilic myocarditis rather than lymphocytic myocarditis; the fourth case report, Thanjan, discusses a patient who did not undergo endomyocardial biopsy, so the type of

[76] *See supra* n. 49.

myocarditis was not determined.[77] Petitioner was unable to offer any literature supporting an association between hypersensitivity reactions and lymphocytic myocarditis.

Petitioner's experts submit that Menactra can cause lymphocytic myocarditis via a hypersensitivity reaction and/or myocardial infiltration of T-cells stimulated by the body's immune response to Menactra. The respondent's experts disagree that Menactra, or any vaccine, can cause lymphocytic myocarditis. However, all the experts agree that a hypersensitivity reaction, which can occur following vaccination, is mainly characterized by eosinophils. In the words of Dr. Yeager, petitioner's experts' arguments are clinically unconvincing and scientifically unsupported. Resp. Ex. E at 3. Based on the medical records, reports, medical literature, and testimony submitted, I find respondent's experts more persuasive and their opinions more consistent with all of literature submitted in this case. Petitioner has failed to provide preponderant evidence to satisfy *Althen* Prong I.

ii. *Althen* Prong Two: Petitioner Has Failed to Provide a Logical Sequence of Cause and Effect Between the Menactra Vaccine and the Vaccinee's Lymphocytic Myocarditis

Having determined that petitioner has not shown that the Menactra vaccine can cause lymphocytic myocarditis, it follows that petitioner cannot show that the Menactra vaccine caused Robert to develop lymphocytic myocarditis.

Petitioner's experts emphasized that Robert had a hypersensitivity reaction to the Menactra vaccine, regardless of the type of myocarditis he suffered. Dr. Waters distinguished "hypersensitivity myocarditis" as a clinical term and "lymphocytic myocarditis" as a histological term. Tr. 76. According to Dr. Waters, a clinical diagnosis of hypersensitivity myocarditis could have a predominantly lymphocytic infiltrate. Tr. 35-36. She suggested that Robert had a Type IV delayed hypersensitivity reaction, stating that Type IV reactions have a wide range of symptoms. Tr. 87. The only support Dr. Waters provided for this opinion was a page from a pathology textbook which stated that a Type IV hypersensitivity reaction was mediated by T-lymphocytes. The remainder of the page was redacted. *See* Pet. Ex. 23. Dr. Waters did not provide any literature associating Type IV hypersensitivity reactions with lymphocytic myocarditis, nor did she provide any literature discussing the presentation and symptoms of a Type IV hypersensitivity reaction.

Dr. Chang agreed with Dr. Waters that myocarditis is a clinical, not a pathological, diagnosis. Tr. 190, 191, 217. He emphasized that not everyone reacts the same way to vaccines; in his opinion, a hypersensitivity reaction could present with eosinophils in some people and lymphocytes in others. Tr. 194, 204-05, 224. Dr. Chang did not submit any literature to support this suggestion. He repeatedly stated that whether a patient had lymphocytic myocarditis or eosinophilic myocarditis or what caused it was of no import to him since his only focus is on the clinical symptoms and treating the patient. Tr. 191, 192, 197, 216, 218. This was a peculiar statement to make during a hearing aimed at determining the cause of Robert's myocarditis.

Dr. Chang's opinion seemingly relied on the temporal relationship between Robert's Menactra vaccination and his death three days later. He determined that Robert had

[77] *See* Pet. Ex. 18, *supra* n.40; Pet. Ex. 21, *supra* n. 36; Pet. Ex. 28, *supra* n.44.

hypersensitivity myocarditis "because…it is acute fulminant myocarditis because the patient died in two or three days." Tr. 210. "The patient died in two or three days after administration of a substance. The much higher likelihood is that that was the cause of inflammation than anything else that has happened to this particular patient." Tr. 210. He agreed that timing was "one of the major supportive evidence (sic) for this being a reaction to the vaccine." Tr. 211.

Neither Dr. Waters nor Dr. Chang explained how, if one were to accept that the vaccine caused Robert to have a hypersensitivity reaction resulting in a fulminant myocarditis and death three days later, he had no other symptoms, such as rash, fever, headache, seizures, vomiting, unexplained weakness, or paresthesia, at any time between July 27, 2012 when he received the vaccination and the time of his death on the afternoon of July 30, 2012. Pet. Ex. 16. In fact, according to petitioner, he was his usual self; he played video games, watched TV, used his Leapfrog, ate, and went to school with no apparent issues.

Respondent's experts, however, submitted that it is not uncommon for people with viral myocarditis to be asymptomatic; Dr. Yeager specifically noted that about 10 percent of unexpected cardiac death is associated with myocarditis. Tr. 108-09. Dr. Yeager did not find Robert's lack of symptoms inconsistent with cases involving other healthy young adults. Tr. 176. The literature supports their opinions that many cases of viral myocarditis are asymptomatic. *See, e.g.,* Resp. Ex. A, Tab 3 at 4 ("Clinical manifestations range from asymptomatic ECG abnormalities to cardiogenic shock…most patients remain entirely asymptomatic"); Resp. Ex. A, Tab 4 at 3 ("Clinical manifestations of acute myocarditis range from non-specific systemic symptoms (fever, myalgia, palpitations or exertional dyspnea") to fulminant haemodynamic collapse"); Resp. Ex. A, Tab 13 at 3 (In a study on cardiac deaths, a "prodromal flu-like illness was reported by half of the subjects" who had myocarditis; the other half of myocarditis deaths did not report symptoms). Respondent's experts postured that Robert suffered from lymphocytic myocarditis which was most likely caused by a virus. Tr. 99-100, 173.

All of the experts in this case are highly credentialed in their respective fields. However, the evidence submitted in this case clearly establishes that Robert's cause of death was lymphocytic myocarditis which is most commonly caused by viral infection. While the Luminex Virus Panel Assay was a source of contention for petitioner, only petitioner's experts relied on the results, which neither actually reviewed, in stating that Robert did not have any viral infection and therefore only the Menactra vaccine could have caused his myocarditis. Without the Luminex results, it is unknown whether Robert was suffering from a viral infection at the time of his death. Even if I disregarded Dr. Folkerth's opinion and testimony, Dr. Yeager would have been a more reliable and stronger expert in this case than Drs. Waters and Chang. To the detriment of petitioner's experts' opinions, the literature unequivocally shows that a hypersensitivity reaction resulting in myocarditis would result in eosinophils on autopsy, even if found in combination with lymphocytes. The presence of eosinophils would result in a diagnosis of eosinophilic myocarditis, not lymphocytic myocarditis. Moreover, both of petitioner's experts were driven by the three-day time frame between vaccination and death, which is not enough to support a logical connection between vaccination and injury. "A proximate temporal association alone does not suffice to show a causal link between the vaccination and the injury." *Grant v. Sec'y of Health & Human Servs*., 956 F.2d 1144, 1148 (Fed. Cir. 1992).

Petitioner has failed to establish Prong II.

iii. *Althen* Prong Three: Petitioner Has Failed to Establish a Proximate Temporal Relationship Between the Menactra Vaccine and the Vaccinee's Lymphocytic Myocarditis

Dr. Chang and Dr. Waters opined that the three-day interval between Robert's receipt of the Menactra vaccination and his death was appropriate for a hypersensitivity reaction. Neither expert explained why three days was an appropriate time frame.

Dr. Folkerth stated that the pattern of inflammation on Robert's autopsy is not consistent with a vaccine reaction. Tr. 109-10. She explained that Robert's autopsy showed that he had lymphocytes in the epicardial fat, the outside layer of the heart, which means that not only the heart, but the tissue around the heart, was involved. Lymphocytes are a marker for chronic inflammation. Tr. 141. "That type of inflammation takes some days to weeks to develop. That's not an acute type of reaction." Tr. 139-40.

Had this been an eosinophilic hypersensitivity reaction to the vaccine, three days between vaccination and death may have been supported by the literature. However, the literature and the autopsy findings in this case support lymphocytic myocarditis and an ongoing process that began prior to Robert's vaccination.

Petitioner has not put forth preponderant evidence supporting a temporal relationship between Robert's development of lymphocytic myocarditis and Menactra vaccine and therefore has failed to satisfy her burden under Prong III.

VII. Conclusion

When petitioners fail to carry their burden, the Secretary is not required to present an alternate explanation for the vaccinee's condition. *De Bazan*, 539 F.3d at 1352. The petitioner in this matter has failed to put forth a prima facie showing of causation; therefore, respondent is not required to demonstrate that a "factor unrelated" was the sole cause of the vaccinee's condition.

This case was very sad, and my sympathies go out to the Yates family. However, petitioner has not put forth preponderant evidence that the Menactra vaccine received by Robert caused him to develop lymphocytic myocarditis which lead to his death and has not therefore demonstrated entitlement to compensation. This case must be dismissed.

In the absence of a timely filed motion for review (see Appendix B to the Rules of the Court), the Clerk shall enter judgment in accordance with this decision.[78]

[78] Pursuant to Vaccine Rule 11 (a), if a motion for review is not filed within 30 days after the filing of the special master's decision, the clerk will enter judgment immediately.

IT IS SO ORDERED.

s/ Mindy Michaels Roth
Mindy Michaels Roth
Special Master